In the United States Court of Federal Claims

OFFICE OF SPECIAL MASTERS

Filed: March 30, 2022

NICOLE TRACY and DANNY STOTLER, on behalf of R.S., their minor child,	*	No. 16-213V
Petitioners,	*	Special Master Sanders
v.	*	
SECRETARY OF HEALTH AND HUMAN SERVICES,	*	Ruling on Entitlement; Pneumococcal Conjugate ("Prevnar 13" or "PCV 13") Vaccine; Transverse Myelitis ("TM"); Molecular Mimicry
Respondent.	*	

Mari Bush, Mari C. Bush, L.L.C., Boulder, CO, for Petitioner.
Althea Davis, United States Department of Justice, Washington, DC, for Respondent.

RULING ON ENTITLEMENT[1]

On February 11, 2016, Nicole Tracy and Danny Stotler ("Petitioners") filed a petition for compensation on behalf of their minor child R.S. pursuant to the National Vaccine Injury Compensation Program.[2] Pet. at 1, ECF No. 1; 42 U.S.C. §§ 300aa-1 to -34 (2012). Petitioners allege that the pneumococcal conjugate ("PCV 13" or "Prevnar 13") vaccine R.S. received on March 18, 2013, caused her to suffer from transverse myelitis ("TM").[3] Pet. at 1.

After carefully analyzing and weighing all the evidence and testimony presented in this case in accordance with the applicable legal standards,[4] I find that Petitioners have provided

[1] This Ruling shall be posted on the United States Court of Federal Claims' website, in accordance with the E-Government Act of 2002, 44 U.S.C. § 3501 note (2012) (Federal Management and Promotion of Electronic Government Services). In accordance with Vaccine Rule 18(b), a party has 14 days to identify and move to delete medical or other information that satisfies the criteria in § 300aa-12(d)(4)(B). Further, consistent with the rule requirement, a motion for redaction must include a proposed redacted Ruling. If, upon review, I agree that the identified material fits within the requirements of that provision, such material will be deleted from public access.

[2] National Childhood Vaccine Injury Act of 1986, Pub L. No. 99-660, 100 Stat. 3755. Hereinafter, for ease of citation, all "§" references to the Vaccine Act will be to the pertinent subparagraph of 42 U.S.C. § 300aa (2012).

[3] Transverse myelitis ("TM") is "myelitis in which the functional effect of the lesions spans the width of the entire cord at a given level." *Dorland's Illustrated Medical Dictionary* 1, 1218 (32nd ed. 2012) [hereinafter "*Dorland's*"]. Myelitis is "inflammation of the spinal cord[.]" *Dorland's* at 1218.

[4] While I have reviewed all of the information filed in this case, only those filings and records that are most relevant to the decision will be discussed. *Moriarty v. Sec'y of Health & Hum. Servs.*, 844 F.3d 1322, 1328

preponderant evidence that the Prevnar 13 vaccine R.S. received on March 18, 2013, was the cause-in-fact of her TM. Accordingly, Petitioners are entitled to compensation and this case shall proceed to the damages phase.

I. Procedural History

Petitioners filed their petition for compensation on February 11, 2016. Pet. at 1. The same day, Petitioners filed R.S.'s immunization record, affidavits, and medical records. Pet'r's Exs. 1–15, ECF Nos. 1-3–1-17. Petitioners filed a statement of completion on March 17, 2016. ECF No. 9. On May 5, 2016, Petitioners submitted an updated medical record and an amended statement of completion. Pet'r's Ex. 16, ECF Nos. 12–13.

Respondent filed his Rule 4(c) report on June 16, 2016, recommending that compensation be denied. Resp't's Report at 1, ECF No. 14. A status conference was held on June 23, 2016, to discuss Respondent's "concern[s] about both whether the Prevnar [13] vaccine could cause [R.S.'s] injuries and whether an alternative cause was actually responsible for [R.S.'s] injuries." Sched. Order, ECF No. 15; *see also* Min. Entry, docketed June 23, 2016. Following the conference, the presiding special master ordered Petitioners to file an expert report. Sched. Order at 1. Prior to filing an expert report, Petitioners submitted updated medical records and an amended statement of completion on December 16, 2016. Pet'r's Exs. 17–21, ECF Nos. 20–21. This case was transferred to me on January 12, 2017. ECF Nos. 22–23.

On February 23, 2017, Petitioner filed an expert report from Lawrence Steinman, M.D., and supporting medical literature. Pet'r's Exs. 22–45, ECF Nos. 25-1–25-5. Respondent filed his responsive expert report from Stephen McGeady, M.D., on June 30, 2017, along with supporting medical literature. Resp't's Exs. A–J, ECF Nos. 29-1–29-10.

Petitioners submitted a supplemental expert report and medical literature on August 28, 2017. Pet'r's Exs. 46–53, ECF Nos. 30-1–30-8. Three days later, Petitioners filed additional medical records and documentation regarding R.S.'s disability status. Pet'r's Exs. 54–58, ECF Nos. 31-1–31-5. Respondent filed a supplemental expert report and medical literature on October 31, 2017. Resp't's Exs. K–S, ECF Nos. 32-1–32-9. Petitioner filed an updated medical record on March 15, 2018. Pet'r's Ex. 59, ECF No. 38-1.

I held a status conference with the parties on May 8, 2018. *See* Min. Entry, docketed May 8, 2018. During the status conference, I discussed the expert reports and noted "areas where the expert reports may benefit from additional clarification[.]" *See* Sched. Order at 1–2, ECF No. 40. Following the conference, I ordered the parties to discuss the case and to file a joint status report indicating how they wish to proceed. *Id.* at 2. On July 18, 2018, Petitioners filed a status report on behalf of both parties and noted that they would like to proceed with additional expert reports. ECF No. 44. The same day, Petitioners filed a supplemental expert report and supporting medical

(Fed. Cir. 2016) ("[w]e generally presume that a special master considered the relevant record evidence even though he does not explicitly reference such evidence in his decision.") (citation omitted); *see also Paterek v. Sec'y of Health & Hum. Servs.*, 527 F. App'x 875, 884 (Fed. Cir. 2013) ("[f]inding certain information not relevant does not lead to—and likely undermines—the conclusion that it was not considered.").

literature. Pet'r's Exs. 60–68, ECF Nos. 45-1–45-10, 46–49. Respondent filed a responsive supplemental report on September 4, 2018, along with supporting medical literature on October 22, 2018. Resp't's Exs. T–Z, ECF Nos. 50-1, 52-1–52-6. On October 29, 2018, Petitioners filed a status report requesting that this case proceed to an entitlement hearing. ECF No. 53.

I scheduled this matter for an entitlement hearing to take place on January 15–16, 2020. Hearing Order, ECF No. 55. Petitioners filed their pre-hearing brief on October 25, 2019. Pet'r's Br., ECF No. 59. The same day, Petitioners filed a status report indicating that they wished to provide an expert report from R.S.'s treating neurologist Teri Schreiner, M.D., and to present her testimony during the hearing. ECF No. 60. I held a status conference with the parties on November 6, 2019, to discuss Petitioners' request. *See* Min. Entry, docketed Nov. 6, 2019. Following the conference, I suspended Respondent's deadline for filing his responsive pre-hearing brief and ordered Petitioners to file their treating physician's report by December 2, 2019. Sched. Order at 2, ECF No. 63. On November 27, 2019, Petitioners filed a status report noting Dr. Schreiner's limited availability on the scheduled dates of the entitlement hearing and requesting it be rescheduled. ECF No. 64. Petitioners filed a written letter from Dr. Schreiner on December 3, 2019. Pet'r's Ex. 71, ECF No. 66-1.

On December 3, 2019, I held a status conference with the parties to discuss Petitioners' request. *See* Min. Entry, docketed Dec. 3, 2019. Following the conference, I ordered Respondent to determine if, after a review of her report, further examination of Dr. Schreiner was necessary. Sched. Order, ECF No. 67. I further ordered Petitioners to file a formal motion requesting a postponement of the entitlement hearing and reinstated Respondent's deadline for filing his responsive pre-hearing brief. *Id.* Petitioners filed their motion to reschedule the entitlement hearing on December 17, 2019. ECF No. 68. The next day, Respondent indicated via e-mail that his responsive brief would not contain new causation theories or counter positions. Informal Comm., docketed Dec. 17, 2019. On December 18, 2019, I denied Petitioners' motion to postpone the entitlement hearing. ECF No. 69.

Petitioners filed an updated medical record on December 19, 2019. Pet'r's Ex. 72, ECF No. 71-1. The next day, Respondent submitted his responsive pre-hearing brief. Resp't's Resp., ECF No. 72. Respondent refiled highlighted medical literature on December 23, 2019. Resp't's Exs. U–GG, ECF Nos. 76-1–76-13. On December 29, 2019, Petitioner filed a YouTube video link exhibit. Pet'r's Ex. 73, ECF No. 78. Petitioner refiled highlighted medical literature exhibits on January 2, 3, and 6, 2020. Pet'r's Exs. 74–95, ECF Nos. 80-1–81-12, 84-1–84-3. The entitlement hearing was held as scheduled on January 15, 2020, in Denver, CO. *See* Min. Entry, docketed Jan. 21, 2020. However, it was not held in its entirety as a result of the presentation of a new theory of causation from Petitioners' expert, Dr. Steinman. *See* Tr. 72–78. I continued the hearing to take the remaining direct testimony of Dr. Steinman. Tr. 80–85. I noted that Dr. Steinman's testimony would serve as a supplemental expert report regarding his new theory of causation, to which Respondent could then respond following the conclusion of the hearing. Tr. 84:22–25, 85:1–23.

Following the entitlement hearing, Petitioners filed the U.S. patent for the Prevnar 13 vaccine on January 17, 2020. Pet'r's Ex. 96, ECF No. 87-1. On January 22, 2020, Respondent filed a status report requesting time to evaluate Petitioners' expert's new theory of causation that was presented during the hearing. ECF No. 88. I held a status conference with the parties on January

23, 2020, to discuss Respondent's request. *See* Min. Entry, docketed Jan. 23, 2020. Following the conference, I ordered Respondent to file a responsive supplemental expert report responding to Petitioners' new theory of causation by March 6, 2020. Non-PDF Order, docketed Feb. 18, 2020. On February 12, 2020, I scheduled the entitlement hearing to resume on April 6–7, 2020. Hearing Order, ECF No. 91.

Respondent submitted medical literature on March 6, 2020. Resp't's Exs. HH–II, ECF Nos. 92-1–92-2. I held a status conference with the parties on March 26, 2020, to discuss the implications of the COVID-19 pandemic. *See* Min. Entry, docketed Mar. 27, 2020. The same day, I cancelled the entitlement hearing and ordered Respondent to submit his supplemental expert report. Non-PDF Order, docketed Mar. 27, 2020.

On April 27, 2020, Respondent filed his supplemental expert report addressing Petitioners' new theory of causation, along with supporting medical literature. Resp't's Exs. JJ–LL, ECF Nos. 93-1–93-3. Petitioners filed a supplemental report and medical literature on May 28, 2020. Pet'r's Exs. 97–100, ECF Nos. 95-1–95-5. On July 15, 2020, Respondent filed an additional supplemental report. Resp't's Ex. MM, ECF No. 96-1. Petitioners submitted a final supplemental report on August 7, 2020. Pet'r's Exs. 101–102, ECF Nos. 98-1–98-2. I scheduled this matter to continue the entitlement hearing on January 14, 2021. Hearing Order, ECF No. 99. The entitlement hearing resumed as scheduled on January 14, 2021. *See* Min. Entry, docketed Jan. 14, 2021.

Following the entitlement hearing, Petitioners filed an opening post-hearing brief on February 26, 2021. Pet'r's Br., ECF No. 102. On March 29, 2021, Respondent filed his post-hearing response brief. Resp't's Resp., ECF No. 103. Petitioners filed their post-hearing reply brief on April 30, 2021. Pet'r's Reply, ECF No. 105. On February 4, 2022, Petitioners filed a notice of additional authority citing recent decisions of special masters as support for their claim. ECF No. 108. This matter is now ripe for consideration.

II. Factual Background

A. Medical Records

R.S. was born full-term on June 13, 2012, and was healthy at birth. Pet'r's Ex. 5 at 6, ECF No. 1-7. R.S. visited James Wigington, M.D., at Salida Family Medicine for her infant examinations. *See* Pet'r's Ex. 5. Dr. Wigington noted a "normal assessment" at R.S.'s one and two-month infant well-child visits. *Id.* at 13, 17. R.S. received her first dose of the Prevnar 13 vaccine during her two-month well-child visit on August 16, 2012. *Id.* at 20–21.

On September 22, 2012, R.S. returned to Dr. Wigington for a cough. *Id.* at 23. He assessed her with acute bronchitis[5] and prescribed Azithromycin[6] and an Albuterol[7] inhaler. *Id.* at 25. R.S. returned two days later and noted that her bronchitis was improving. *Id.* at 26–28. On October 8, 2012, R.S. returned to Dr. Wigington with complaints of "wheezing and cough[ing]" that were "just not getting any better." *Id.* at 29. Her wheezing was reported as worse in the morning. *Id.* Petitioners noted R.S. had a runny nose that was "mucousy." *Id.* Dr. Wigington assessed R.S. with bronchitis and prescribed prednisolone.[8] *Id.* at 31. R.S. underwent a chest X-ray on October 9, 2012, which showed "mild thickening in the central peribranchial soft tissue." *Id.* at 32. The impression was "[m]ild [reactive] airway disease.[9] No infiltrates." *Id.* R.S. returned for a four-month well-visit on October 24, 2012, and her assessment was normal. *Id.* at 33–35. She received the second dose of the Prevnar 13 vaccine during this visit. *Id.* at 36.

R.S. returned to Dr. Wigington on November 9, 2012, with complaints of post-nasal drip, nasal blockage, cough, wheezing, and "acting fussy." *Id.* at 37. Dr. Wigington assessed her with "bronchiolitis infectious"[10] and prescribed Azithromycin and continued nebulizers. *Id.* at 39.

On December 11, 2012, R.S. presented for her six-month well-child visit. *Id.* at 40. Dr. Wigington's assessment of R.S. was normal except for nasal congestion. *Id.* at 42. He prescribed Claritin.[11] *Id.* at 43. Two days later, on December 13, 2012, R.S. returned to Dr. Wigington with complaints of a cough that was described as "consistent again." *Id.* at 44. Petitioners noted that R.S. had a runny nose and that R.S. "continue[d] to wheeze and . . . up [to] 3–4 times NOC and seem[ed] to 'gasp' for air." *Id.* Dr. Wigington assessed R.S. with "[r]eactive airway disease and probably [upper respiratory infection ("URI")]." *Id.* at 46. Dr. Wigington also noted that R.S. "[p]ossibly had [respiratory syncytial virus ("RSV")[12]] during the summer," and "since then has

---

[5] Bronchitis is "inflammation of a bronchus or bronchi; there are both acute and chronic varieties. Symptoms usually include fever, coughing, and expectoration." *Dorland's* at 252.

[6] Azithromycin is "an antibiotic, derived from erythromycin, that inhibits bacterial protein synthesis, effective against a wide range of gram-positive, gram-negative, and anaerobic bacteria; used in the treatment of mild to moderate infections caused by susceptible organisms, administered orally and intravenously." *Dorland's* at 187.

[7] Albuterol is "a β-adrenergic agonist . . . ; administered by inhalation as a bronchodilator for the treatment and prophylaxis of bronchospasm associated with . . . chronic obstructive airway disease, the treatment of asthma-associated bronchospasm, and the prophylaxis of exercise-induced bronchospasm." *Dorland's* at 45.

[8] Prednisolone is "a synthetic glucocorticoid derived from cortisol, administered orally in replacement therapy for adrenocortical insufficiency and as an anti-inflammatory and immunosuppressant in a wide variety of conditions." *Dorland's* at 1508.

[9] Reactive airway disease is "any of several conditions characterized by wheezing and allergic reactions; the most commons ones are asthma, bronchiolitis, and chronic obstructive lung disease." *Dorland's* at 542.

[10] Bronchiolitis infectious refers to bronchitis. *See supra,* note 5.

[11] Claritin is the "trademark preparation of loratadine." *Dorland's* at 368. Loratadine is "a nonsedating antihistamine . . . with no significant antimuscarinic effects; used for the treatment of allergic rhinitis and chronic idiopathic urticaria and as a treatment adjunct in asthma, administered orally." *Id.* at 1074.

[12] Respiratory syncytial virus ("RSV") refers to "any of a group of viruses belonging to the genus *Pneumovirus,* isolated originally from chimpanzees . . . . In humans, they cause respiratory disease that is particularly severe in infants, in whom it causes bronchiolitis [] and sometimes pneumonia." *Dorland's* at 2064.

had recurrent URIs with coughing and wheezing." *Id.* Dr. Wigington prescribed R.S. liquid Albuterol instead of nebulizers. *Id.*

On January 28, 2013, R.S. returned to Dr. Wigington for evaluation of her cough. *Id.* at 49. Petitioners noted that R.S. was "feeling congested in the chest," had a "cough [that was] hacking" in nature and "sound[ed] loose." *Id.* Dr. Wigington assessed R.S. with acute bronchitis and noted her history of recurrent and protracted URIs. *Id.* at 49–51. He prescribed prednisolone, a vaporizer, and Albuterol nebulizer. *Id.* at 51.

Due to her recurrent respiratory issues, R.S. presented to pulmonary specialist Deborah Liptzin, M.D., on March 8, 2013. *Id.* at 52. Dr. Liptzin noted that R.S. had a history relevant for "recurrent cough/wheeze with respiratory illnesses[.]" *Id.* at 53. She noted a "high suspicion for asthma[]"[13] but that "[A]lbuterol and steroids [were] not helping her wheeze/cough as well as inspiratory wheeze would go against that." *Id.* Dr. Liptzin recommended a treatment course consistent with asthma, including Flovent[14] and Albuterol nebulizers. *Id.* at 54.

R.S. returned to Dr. Wigington for her nine-month well-child visit on March 18, 2013. *Id.* at 56. He noted that R.S.'s physical examination and development were normal. *Id.* R.S. received her third dose of the Prevnar 13 vaccine during this visit. *Id.* at 59.

On April 1, 2013, R.S. presented to the emergency room for complaints of a sudden onset of decreased movement of her lower extremities, lethargy, and weakness. Pet'r's Ex. 8 at 2, ECF No. 1-10. Petitioners noted that R.S. had URI symptoms for more than one week, including a cough and runny nose. *Id.* at 2–3. The attending physician Richard Ruiter, M.D., ordered lab work, a chest X-ray, and head CT, which yielded normal results. *Id.* at 4. Dr. Ruiter's final impression of R.S. was a URI and lethargy, and he discharged R.S. home. *Id.* at 3.

The following day, on April 2, 2013, R.S. presented to a different emergency room. Pet'r's Ex. 9 at 2, ECF No. 1-11. Petitioners' chief complaint was that "[t]here is something not right" with R.S. *Id.* They stated that they picked R.S. up from daycare after the facility called and told them that R.S. was "lethargic." *Id.* Petitioners noted that R.S. was "alert," but that "any time they tr[ied] to move [R.S.] or change her diaper, she seem[ed] to cry out in pain." *Id.* They reported that, at a different ER the previous day, "a CT of [her] head, chest X-ray, CBC, renal electrolytes, and urinalysis . . . were reported . . . as normal." *Id.* Petitioners reported that R.S. "ha[d] not been wanting to eat or drink very much since yesterday." *Id.* On examination, R.S. did "not move her upper or lower extremities[,]" although "[s]he seem[ed] to have good tone in both upper and lower extremities." *Id.* at 3. The attending ER physician Gregory Collins, M.D., noted that R.S. "seem[ed] to whimper and cry with any movement" and "prefer[ed] to lie in a supine position."

[13] Asthma is "recurrent attacks of paroxysmal dyspnea, with airway inflammation and wheezing due to spasmodic contraction of the bronchi. Some cases are allergic manifestations in sensitized persons; others are provoked by factors such as vigorous exercise, irritant particles, psychological stresses, and others." *Dorland's* at 168.

[14] Flovent is the "trademark preparation of fluticasone propionate." *Dorland's* at 719. Fluticasone propionate is "a synthetic corticosteroid used topically as an anti-inflammatory and antipruritic in treatment of corticosteroid-responsive dermatoses, intranasally in treatment of allergic rhinitis, other inflammatory nasal conditions, and nasal polyps, and by inhalation in maintenance treatment of asthma." *Id.* at 722.

Id. R.S. underwent a lumbar puncture ("LP"), which showed a mildly low glucose level at 39, a protein level of 48, and red blood cells. *Id.* She also underwent a cervical spine MRI, which showed a "[d]iffuse abnormal signal and mild expansion of the cervical and upper thoracic spinal cord, from C2 d[own] to about T4 level." *Id.* at 13. Dr. Collins noted that "[t]his favor[ed] an acute inflammatory process of the cervical spine, involving predominantly the central gray matter structures and posterior columns. Idiopathic [TM] c[ould] be considered, as well as additional acute inflammatory encephalomyelitis/myelitis."[15] *Id.* He admitted R.S. for further evaluation. Pet'r's Ex. 10 at 44, ECF No. 1-12. At the time, the on-call pediatric attending, Elizabeth Martin, M.D., noted that R.S. "has had [two] normal [white blood counts], one low-grade fever at home[,] but no other documented fever and no focal sign of infection." *Id.*

The next day, R.S. underwent a neurological evaluation with Brian Grabert, M.D. *Id.* at 47. Dr. Grabert's examination revealed "no movement in [R.S.'s] upper or lower extremities except to touch and then she had withdrawal." *Id.* at 48. Dr. Grabert also noted "flaccid muscle tone in [R.S.'s] upper extremities and markedly decreased tone in [her] lower extremities." *Id.* Dr. Grabert wrote that R.S. "seemed to have some synesthesia, meaning with touching her upper extremities, she started to whimper, less so in the lower extremities." *Id.* Dr. Grabert wrote that R.S.'s MRI was "consistent with [TM] with multiple segment involvement from C1 down to T4." *Id.* at 48, 858. R.S.'s infectious disease work-up was negative. *Id.* at 858–59. He assessed R.S. with TM and treated her with high dose Solumedrol[16] and one IVIG treatment. *Id.* After receiving this course of treatment, Dr. Grabert noted that R.S. was "regaining some strength" and had "daily improvements in her strength, tone, and abilities." *Id.* at 859. R.S. was discharged on April 9, 2013, with a recommendation for physical therapy ("PT") and prescriptions for a sixteen-day Orapred[17] taper, Prevacid Solutab,[18] and gabapentin.[19] *Id.* at 857–59.

On April 10, 2013, R.S. followed up with Dr. Wigington. Pet'r's Ex. 5 at 63. Petitioners reported that upon discharge the day before, R.S. had "good head movement and [was] able to move [her] arms a little bit[,] but [she] still [had] no movement from her legs." *Id.* Dr. Wigington's assessment of R.S. was TM, and he noted R.S.'s plans to begin PT. *Id.* at 65.

R.S. returned to the ER for admission on April 17, 2013, for the purpose of placement of a central venous catheter and treatment with plasmapheresis.[20] Pet'r's Ex. 11 at 1, ECF No. 1-13. The attending physicians noted that R.S.'s TM was "most-likely post-infectious[.]" *Id.* at 3. A

[15] Encephalomyelitis is "inflammation involving both the brain and the spinal cord." *Dorland's* at 613.
[16] Solumedrol is the "trademark preparation of methylprednisolone sodium succinate." *Dorland's* at 1731. Methylprednisolone sodium succinate is "the 21-succinate sodium salt of methylprednisolone, having actions and uses similar to those of the base; it is highly soluble in water and is chiefly used for the rapid achievement of high blood levels of methylprednisolone in short-term emergency treatment; administered by intramuscular or intravenous injection." *Id.* at 1154.
[17] Orapred is a brand name for prednisolone. *Dorland's* at 1508; *see also supra,* note 8.
[18] A Prevacid Solutab is a water-soluble form of Prevacid. Prevacid is the "trademark preparation of lansoprazole." *Dorland's* at 1513. Lansoprazole "acts as a proton pump inhibitor; used to inhibit the secretion of gastric acid for the symptomatic treatment of duodenal and gastric ulcers . . . ." *Id.* at 1004.
[19] Gabapentin is "an anticonvulsant that is . . . used as adjunctive therapy in the treatment of partial seizures and the management of postherpetic neuralgia; administered orally." *Dorland's* at 753.
[20] Plasmapheresis is "the removal of plasma from withdrawn blood, with re-transfusion of the formed elements into the donor[.]" *Dorland's* at 1456.

repeat MRI conducted on April 23, 2013, showed "[i]nterval improvement in edema throughout the cervical spinal cord with only residual signal abnormality involving the dorsal columns of the spinal cord from C2–C3 through C6–C7[, with no] abnormalities following contrast . . . ." Pet'r's Ex. 5 at 85. Her diagnoses included TM, neurogenic bowel and bladder,[21] quadriparesis,[22] and neuropathic pain. *Id.* at 90. During treatment, R.S. "had significant return of motor function . . . ." Pet'r's Ex. 11 at 6. R.S. completed her course of treatment on April 24, 2013, and she was transferred to inpatient rehabilitation. *Id.*

After several weeks of inpatient rehabilitation, R.S. "showed improvements with all mobility tasks[,] as she was able to roll from supine [position] to her side with minimal assistance." *Id.* at 269. The attending physician noted that R.S. also "showed improved trunk stability while in supported standing [position] by pushing up with her arms and maintaining the position well." *Id.* R.S. "demonstrated improved ability to reach outside her base of support and reach over [her] head to get toys while in [a] sitting [position]." *Id.* R.S. was discharged from inpatient rehabilitation on May 17, 2013. *Id.*

On June 21, 2013, R.S. presented to Dr. Wigington for her twelve-month well-visit. Pet'r's Ex. 5 at 126. He noted that R.S. was "making very good progress," although she was "still hav[ing] lower extremity . . . and some upper extremity deficits." *Id.* Petitioners reported that R.S. "[could] move [her] legs . . . [and] roll over[,]" but she was unable to "crawl[] or stand[.]" *Id.* at 126, 129. Dr. Wigington's assessment of R.S. was normal. *Id.* at 129. He indicated that "[n]o immunizations were given [to R.S.] at this [visit]" because Petitioners were "concerned that immunizations had [a] part in [her TM]." *Id.*

R.S. followed up with rehabilitation specialist Elizabeth Knight, M.D., on June 28, 2013. *Id.* at 141. Petitioners noted that R.S. was receiving two PT and occupational therapy ("OT") visits each week and "doing exercises at home . . . ." *Id.* They reported that R.S. was "still on Neurontin,[23] but only taking it twice per day." *Id.* Petitioners continued that R.S. was "[a]ble to bear weight through her legs." *Id.* R.S.'s father reported that her "[a]rms [were] almost 100%." *Id.* Petitioners indicated that R.S. was "starting to commando crawl, and if placed in a hands/knees position, [she would] hold that position and even rock back and forth." *Id.* She could also "sit unassisted, and [could] even play with a toy in both hands." *Id.* Dr. Knight's assessment of R.S. was "[twelve]-month-old girl with history of [TM], who is making nice functional gains." *Id.* at 143. She advised R.S. to continue with her therapy regimen and to follow up in three months. *Id.* at 144. R.S. followed up with neurologist Dr. Schreiner following her inpatient admission on July 12, 2013. *Id.* at 151. Dr. Schreiner did not opine as to the cause of R.S.'s TM during this visit. *Id.* at 151–57.

On October 11, 2013, R.S. had a follow-up with rehabilitation specialist Michael Dichiaro, M.D. *Id.* at 164. Dr. Dichiaro wrote that R.S. was "[p]rogressing towards crawling – [she could] bring [her] knees to [her] elbows to crawling position. [She was] army crawling, [and had] increased movements in [her] legs." *Id.* He also noted improving tone in R.S.'s bilateral lower

[21] Neurogenic bowel and bladder refers to "any condition of dysfunction of the urinary bladder [or bowel] caused by a lesion of the central or peripheral nervous system." *Dorland's* at 222.
[22] Quadriparesis is "muscular weakness affecting all four limbs[.]" *Dorland's* at 1565.
[23] Neurontin is the "trademark for preparations of gabapentin." *Dorland's* at 1268; *see also supra,* note 19.

extremities. *Id.* at 167. Dr. Dichiaro indicated that R.S. was "making nice gains" with her TM. *Id.* He recommended continued PT and OT, and to follow up in three months. *Id.*

The same day, R.S. presented for a neurological follow-up with Dr. Schreiner. *Id.* at 168. Petitioners stated that they "d[id] not think that [R.S. was] feel[ing] pain in her legs, but they [thought] that she [was] feel[ing] pressure." *Id.* at 169. They also noted that R.S. was '"stiff' when she [woke up in the morning], but not during the day." *Id.* Dr. Schreiner wrote that R.S.'s TM was "likely idiopathic." *Id.* at 172. She indicated that R.S. "continue[d] to have impressive recovery of function[,]" and that, while "[t]here [was] some question of sensory disturbance, . . . it [did] not appear to be limiting [R.S.'s] progress." *Id.* She also noted "no evidence of bowel/bladder dysfunction," but that R.S. "will be seen again by urology . . . ." *Id.* Dr. Schreiner recommended vaccinating R.S., but also noted that R.S. should "avoid live virus vaccines." *Id.*

R.S. returned to Dr. Schreiner on April 21, 2014. *Id.* at 212. Petitioners told Dr. Schreiner that R.S. was "making good progress[,]" and "no longer [gave] the indication of pain in her legs." *Id.* at 213. They continued that R.S. was talking and had normal bowel function. *Id.* They also reported that they would "begin to wean [R.S. off] the . . . Neurontin[]" that night. *Id.* On examination, R.S. had decreased upper extremity reflexes, but exhibited normal tone and strength. *Id.* at 216. She also exhibited increased lower extremity reflexes with up-going toes, along with "[s]ome weakness and spasticity when standing[.]" *Id.* Dr. Schreiner's impression was that R.S. "continue[d] to have impressive recovery of function . . . [and her s]ensory disturbance [had] improved." *Id.* Dr. Schreiner "agree[d] with weaning [the] . . . Neurontin," and recommended a dose of Lipoic acid[24] at 300mg. *Id.*

On August 26, 2014, R.S. followed up with rehabilitation specialist Dr. Dichiaro. *Id.* at 238. Petitioners stated that R.S. was "continuing to improve," and that she had "no recent illnesses or hospitalizations." *Id.* They reported that R.S. was "[s]tarting to walk short distances with a push toy or without [supra-malleolar orthosis ("SMO")].[25] [She was t]alking in sentences. [Her] arms [were] close to normal in strength and coordination." *Id.* Dr. Dichiaro noted that R.S. had "some [muscle] tone in [her] lower extremities, and [was] variable, improving. [R.S. was] tight in the morning, but work[ed] through it quickly, [within five] minutes." *Id.* at 239. Petitioners noted that R.S. was still taking "Neurontin .5ml at night," but that they "[had] missed a few doses without any difference." *Id.*

On October 25, 2014, R.S. returned to Dr. Wigington with complaints of a deep cough, wheezing, and loss of appetite for one day. *Id.* at 252. His examination of R.S. revealed no nasal discharge or sinus tenderness, but he heard wheezing upon listening to her lungs. *Id.* at 254. Dr.

---

[24] Lipoic acid is "a necessary cofactor of the pyruvate dehydrogenase, branched-chain α-keto acid dehydrogenase, and α-ketoglutarate dehydrogenase complexes; it contains a reactive disulfide group that can bind and transfer reaction intermediates . . . It is used as a dietary supplement for its antioxidant properties." *Dorland's* at 1062.

[25] "SMO" stands for "supra-malleolar orthosis," which "supports the leg just above the anklebones or malleoli." Scheck & Siress, *SMO (Supra-Malleolar Orthosis),* PROSTHETICS, ORTHOTICS, PEDORTHICS https://www.scheckandsiress.com/wp-content/uploads/2016/08/SMO-JM.pdf (last visited Feb. 18, 2022). It is "often worn by children" and "is designed to maintain a vertical, or neutral heel while also supporting the three arches of the foot. This can help improve standing, balance and walking." *Id.* at 1.

Wigington assessed R.S. with bronchiolitis infectious, and noted that, "[w]ith [R.S.'s] history of [TM, he would] treat aggressively." *Id.* at 255. He prescribed a course of Azithromycin. *Id.*

From October 29 to October 31, 2014, R.S. was admitted at the hospital for "increased cough and hypoxia[26] at home[.]" *Id.* at 269. A chest CT conducted in the ER revealed mild pulmonary edema[27] and severe central airway disease. *Id.* at 256–57. R.S. also tested positive for RSV. *Id.* at 261, 269. She was admitted for IV fluids, oxygen, and nebulizer treatments. *Id.* at 269. During her treatment course, R.S. "stabilized, but continued to have significant rhonchi[28] bilaterally and some left-sided rows." *Id.* R.S. was "started on IV Solumedrol and on the morning of discharge[,] her breath sounds were definitely improved with decreased rhonchi and no audible rales." *Id.* She was discharged home on Prelone syrup[29] and Albuterol nebulizers. *Id.* R.S.'s discharge diagnoses included RSV bronchiolitis, reactive airway disease, and "ongoing lower extremity weakness secondary to prior [TM]." *Id.*

R.S. presented to pulmonologist Paul Stillwell, M.D., on December 2, 2014. *Id.* at 286. Petitioners noted that R.S. got "sick every [three] weeks, with recovery in between. She [got] a runny nose with or without fever that lead [sic] to cough and wheeze and dyspnea." *Id.* Petitioners expressed "concern[] that [R.S. was] too sick too often." *Id.* Dr. Stillwell's impression included asthma, restrictive lung disease, and TM, which was noted to be "improving." *Id.* at 287–88. He recommended increased asthma medications and Albuterol treatments. *Id.*

On January 26, 2015, R.S. returned to Dr. Dichiaro for a follow-up. Pet'r's Ex. 12 at 74, ECF No. 1-14. Dr. Dichiaro noted that R.S. was "doing very well . . . [with no] major illnesses, [and Petitioners] . . . noted that [R.S. was] continuing to get stronger." *Id.* On examination, Dr. Dichiaro wrote that R.S. had poor truncal tone, right ankle clonus,[30] and she was dragging her toes bilaterally. *Id.* at 76. He recommended a gait analysis and continued PT/OT. *Id.* at 77.

R.S. presented to Dr. Schreiner for a neurological follow-up on May 11, 2015. *Id.* at 94. Dr. Schreiner wrote that R.S. was "weaker on [her] right" side and was walking with a walker in addition to her orthotics. *Id.* On examination, she noted that R.S. had increased tone on her right greater than left side, and there was no evidence of sensory disturbance. *Id.* at 97. She indicated that R.S. was scheduled to receive a Botox[31] injection the following week. *Id.* at 94. Dr. Schreiner's

---

[26] Hypoxia is the "reduction of oxygen supply to tissue below physiologic levels despite adequate perfusion of the tissue by blood." *Dorland's* at 908.

[27] Edema is "the presence of abnormally large amounts of fluid in the intercellular tissue spaces of the body, usually referring to subcutaneous tissues. It may be localized (as from venous obstruction, lymphatic obstruction, or increased vascular permeability) or systemic (as from heart failure or renal disease)." *Dorland's* at 593.

[28] Rhonchus is a "sound . . . consisting of a dry, low-pitched, snore-like noise, produced in the throat or bronchial tube due to a partial obstruction such as by secretions." *Dorland's* at 1642.

[29] Prelone syrup is a "trademark preparation of prednisolone." *Dorland's* at 1508; *see also supra,* note 8.

[30] Clonus is the "alternate muscular contraction and relaxation in rapid succession. 2. a continuous rhythmic reflex tremor initiated by the spinal cord below an area of spinal cord injury, set in motion by reflex testing." *Dorland's* at 373.

[31] Botox is "the trademark for preparations of onabotulinumtoxin A." *Dorland's* at 241. Onabotulinumtoxin A is "a preparation of botulinum toxin type A, purified from the neurotoxin type A complex produced by *Clostridium botulinum* type A and consisting of the neurotoxin and several accessory proteins. It is

impression was that R.S. was "progressing nicely, but ha[d] morbidity of lower extremity spasticity, [and] weakness." *Id.* at 97. She documented Petitioners' plan for R.S. to attend "[i]ntensive rehab[ilitation] at Kennedy Krieger in June [of 2015]." *Id.* at 98.

R.S. presented for an intensive rehabilitation evaluation with Devika Bhushan, M.D., at the Kennedy Krieger Institute on June 1, 2015. Pet'r's Ex. 13 at 1, ECF No. 1-15. Dr. Bhushan noted that R.S. "experienced a viral respiratory illness and got [the] Prevnar [13 vaccination] in the period leading up to her [symptom] presentation." *Id.* at 65. She wrote that R.S. had "great gross and fine motor control over her trunk and bilateral arms. She [was] working on walking using a walker." *Id.* at 1. Dr. Bhushan indicated that "[R.S.] underwent Botox treatment of her hip flexors, adductors, and hamstrings, which were previously spastic, but now have normal [range of motion ("ROM")]." *Id.* Dr. Bhushan noted that the main goal of R.S.'s rehabilitation was increasing R.S.'s walking ability. *Id.* During her admission, R.S. "received comprehensive care by nursing, social work, pediatrics, child life, education, neuropsych[ology], behavioral psych[ology], OT, PT, speech, and nutrition." *Id.* at 66. By the time of her discharge on June 13, 2015, R.S.'s upper extremities and trunk muscle tone, bulk, and strength were all within normal limits. *Id.* at 65–66. She had slightly diminished lower extremity muscle tone. *Id.* at 66. R.S. was "able to ambulate with [the] help of [a] walker, but sometimes by dragging [her] toes and/or crossing one leg in front of [the] other . . . ." *Id.*

On June 9, 2015, R.S. presented to neuro-immunologist Carlos Pardo, M.D. for an evaluation. Pet'r's Ex. 14 at 1, ECF No. 1-16. Dr. Pardo reviewed R.S.'s history and conducted a neurological examination. *Id.* at 1–3. Dr. Pardo wrote that "the major limitation now is the presence of spastic paraparesis."[32] *Id.* at 3. He noted that "it is very clear that [R.S.] experienced myelopathic syndrome that left her with a spastic paraparesis." *Id.* He recommended aggressive PT and rehabilitation. *Id.*

R.S. returned to Dr. Wigington for her three-year well-child visit on September 10, 2015. Pet'r's Ex. 5 at 306. In regard to R.S.'s TM, Petitioners stated that they "thought [it] to be vaccine induced." *Id.* They reported that R.S. had been seen by a rehabilitation specialist, and it was believed that she would be able to walk eventually. *Id.* R.S. received additional Botox injections on December 9, 2015. Pet'r's Ex. 18 at 4, ECF No. 20-2.

The next day, R.S. followed up with Dr. Stillwell for her asthma and restrictive lung disease. *Id.* at 15, 18. He noted that he was "happy [with] how well [R.S.] ha[d] done since [her] last visit." *Id.* at 18. Dr. Stillwell wrote that R.S. had an "ongoing recovery of function" related to her weakness from TM. *Id.* at 15–16.

On March 17–19, 2016, R.S. was hospitalized for a "potential altered mental status" and viral symptoms, such as fever, vomiting, and ear and throat pain. *Id.* at 32, 39, 42. The attending physician noted that R.S. had an "extensive workup . . . which was unrevealing of [an] etiology for [her] altered mental status." *Id.* Her examination was normal absent a "barky" cough. *Id.* at 37. The attending physician wrote that she "[d]oubt[ed it was] meningitis or encephalitis . . . [or]

administered intramuscularly to prevent chronic migraine; to treat cervical dystonia, upper limb spasticity, strabismus, and blepharospasm; and to temporarily improve the appearance of glabellar lines. It is administered subcutaneously to treat severe primary axillary hyperhidrosis." *Id.* at 242.

[32] Paraparesis is "partial paralysis of the lower limbs." *Dorland's* at 1379.

recurrence of [TM] at this time based on [R.S.'s] exam." *Id.* at 32, 35. She wrote that a viral illness was a "likely etiology, as [R.S. was] improving, now afebrile . . . and [her white blood count] would suggest viral suppression." *Id.* at 32–33. R.S. was diagnosed with an upper respiratory "symptom," potential for altered mental status, and acute otitis media[33] and was prescribed antibiotics. *Id.* at 34.

R.S. received Botox injections on March 29, 2016. *Id.* at 89. Dr. Dichiaro noted that R.S.'s "[t]one [had] increased to [both] hamstrings and hip adductors." *Id.* at 89–90. She continued to receive Botox injections throughout 2016. Pet'r's Ex. 21 at 28–29, ECF No. 20-5.

R.S. followed up with Dr. Schreiner on May 16, 2016. Pet'r's Ex. 55 at 10, ECF No. 31-2. Dr. Schreiner described R.S.'s hospitalization in March of 2016 and wrote that R.S. "became very ill and had recurrence of weakness. As she recovered from her illness, her weakness improved." *Id.*; *see also* Pet'r's Ex. 59 at 114, ECF No. 38-1. On examination, R.S. exhibited weakness in her lower extremities, greater on the right than left side, but "[n]o clubbing,[34] cyanosis,[35] or edema." Pet'r's Ex. 55 at 12. Dr. Schreiner also noted "increased tone [greater on the right than left] with tight adductors . . . normal tone in upper extremities[and s]ome weakness and spasticity when standing[.]" *Id.* at 13. Included in Dr. Schreiner's impression was "residual [bilateral lower extremity] spasticity and weakness." *Id.* Dr. Schreiner advised R.S. to follow up in one year. *Id.*

R.S. returned to the Kennedy Krieger Institute for inpatient rehabilitation from June 20 – July 2, 2016. Pet'r's Ex. 19 at 1, 34, ECF No. 20-3. R.S.'s goal for rehabilitation was "to improve functioning status post spinal cord injury secondary to [TM]." *Id.* at 1. Occupational therapist Samantha Hughes, D.O., indicated that R.S. continued to use a rolling walker, bilateral forearm crutches, and leg braces. *Id.* at 2; *see also* Pet'r's Ex. 54 at 2, ECF No. 31-1. She wrote that R.S. was "able to stand with single or bilateral upper extremity support and supervision[.]" Pet'r's Ex. 19 at 4. R.S.'s upper extremity strength and ROM were within normal limits. *Id.* R.S.'s lower extremity tone was noted as "slightly low[.]" *Id.* at 10. She could dress herself with "at best minimal assistance." *Id.* at 6–7. R.S. continued to receive PT treatment for her weakness and "gross motor development" throughout 2016 and 2017.[36] *See, e.g.*, Pet'r's Ex. 56, ECF No. 31-3.

R.S. followed up with Dr. Dichiaro on February 10, 2017. Pet'r's Ex. 55 at 81. He noted that her TM was "making nice gains[.]" *Id.* Dr. Dichiaro noted that R.S. was no longer using a walker, had increased bilateral lower extremity tone, and was "working on walking with one

[33] Otitis media is "inflammation of the middle ear; subtypes are distinguished by length of time from onset *(acute* versus *chronic)* and by type of discharge *(serous* versus *suppurative).*" *Dorland's* at 1351.

[34] Clubbing is "a digital deformity produced by proliferation of the soft tissues about the terminal phalanges of the fingers or toes, with no constant osseous changes; seen in various types of chronic disease of the thoracic organs." *Dorland's* at 375.

[35] Cyanosis is "a bluish discoloration, especially of the skin and mucous membranes due to excessive concentration of deoxyhemoglobin in the blood." *Dorland's* at 452.

[36] While I have reviewed all of the records filed in this case, I have addressed only the medical records I have deemed relevant to this Decision. *Moriarty v. Sec'y of Health & Hum. Servs.*, 844 F.3d 1322, 1328 (Fed. Cir. 2016) ("We generally presume that a special master considered the relevant record evidence even though he does not explicitly reference such evidence in his decision.") (citation omitted); *see also Paterek v. Sec'y of Health & Hum. Servs.*, 527 F. App'x 875, 884 (Fed. Cir. 2013) ("Finding certain information not relevant does not lead to—and likely undermines—the conclusion that it was not considered.").

crutch." *Id.* Regarding R.S.'s gait, he noted that she walked "primarily on [her] toes, dragging [her] toes bilaterally[.]" *Id.* at 83. Dr. Dichiaro's assessment included lower extremity weakness. *Id.* R.S. received Botox injections during this visit. *Id.* at 84; *see also* Pet'r's Ex. 59.

On August 10, 2017, R.S. returned to Dr. Schreiner for a follow-up. Pet'r's Ex. 59 at 112. Dr. Schreiner noted that R.S. continued to "make gains, but has residual [bilateral lower extremity] spasticity and weakness." *Id.* She wrote that R.S. was able to walk with the use of bilateral walking sticks. *Id.* at 117. She also noted that R.S. had a wide-based gait "with pelvic tilt[ing] and flinging motion of [her] legs." *Id.*

R.S. sought treatment for her TM throughout 2018.[37] As of August 14, 2019, R.S. was still in the care of Dr. Schreiner. Pet'r's Ex. 72 at 27, ECF No. 71-1. Dr. Schreiner described R.S.'s TM as "idiopathic [TM] at [ten] months of age." *Id.* She indicated that she would be writing a letter on R.S.'s behalf for the Program. *Id.* Dr. Schreiner noted that R.S. still had residual bilateral lower extremity weakness and was receiving Botox injections. *Id.* at 6, 27. Dr. Schreiner wrote that R.S. had a "stunningly good" physical therapist, who she saw two times per week, along with receiving PT at school. *Id.* at 28. Petitioner has not filed any additional medical records.

B. Petitioners' Affidavits & Fact Testimony

Petitioners submitted two affidavits in support of their petition and Ms. Nicole ("Niki") Tracy testified at the entitlement hearing.[38] *See* Pet'r's Exs. 1, 2, ECF Nos. 1-3, 1-4; *see also* Tr. 12–45. The first of Petitioners' affidavits was authored by Ms. Tracy, R.S.'s mother. Pet'r's Ex. 1 ¶ 1. Ms. Tracy described R.S.'s health both pre and post vaccination consistent with R.S.'s medical records. *Id.* ¶¶ 12–51. Ms. Tracy averred that she and her husband "had no concerns about [R.S.'s] health or development during [R.S.'s] early months." *Id.* ¶ 15. She testified that R.S. was "able to use her arms and legs well[]" and she did not have "[a]ny problems . . . with her bladder or bowel[.]" Tr. 16:23–25, 17:1–4. She noted R.S.'s history of pulmonary issues and recurrent bronchitis. Pet'r's Ex. 1 ¶¶ 18, 19, 22, 23, 25, 26. Ms. Tracy testified that based on her interactions with R.S.'s treaters, R.S.'s asthma and respiratory illnesses were considered "separate and apart from the [TM.]" Tr. 17:11–15.

Ms. Tracy wrote that "[a]s of March 18, 2013 [the day of R.S.'s Prevnar 13 vaccination], . . . R.S. was beginning to crawl, could hold her own weight while standing[,] hold[] onto a table or object, was sitting unassisted, and was able to feed herself with her fingers." Pet'r's Ex. 1 ¶ 28. She testified that in the two weeks following R.S.'s vaccination, "[s]he was great. Nothing was out of the norm." Tr. 20:8–14. Ms. Tracy described the date of onset and wrote that "April 1, 2013[,] began as other days in [Petitioners'] household. R.S. woke up, had breakfast[,] and went to daycare[.]" Pet'r's Ex. 1 ¶ 31. She continued that "[a]t 4:45, [her] day care [sic] provider called [her] and told [her that the provider] was worried about R.S." *Id.* Specifically, the provider told Ms. Tracy that R.S.'s "eyes were glassy, she cried whenever she was touched[,] and she was unable to bear any weight on her legs." *Id.* Ms. Tracy wrote that when she arrived at the daycare, R.S. was "limp . . . [and s]he screamed in pain as [Ms. Tracy] tried to buckle her into her car seat." *Id.*

[37] *See id.*

[38] At the time of the entitlement hearing on January 15, 2020, Ms. Tracy testified as "Nicole Stotler." However, her affidavit was drafted as "Nicole Tracy" so I will refer to her as such throughout this section.

¶ 32. Ms. Tracy testified that R.S.'s condition was "very different" than anything she had experienced with R.S.'s illnesses. Tr. 22:23–24. She described R.S.'s initial ER evaluation at a local hospital that night and noted that "[w]hen the evaluation was done . . . R.S. was extremely lethargic but would call out every time she was moved." Pet'r's Ex. 1 ¶ 34. Ms. Tracy continued that R.S.'s "cries were becoming softer[]" and she was "hardly vocal." *Id.* She also noted that R.S. was "weak and no longer moving her arms." *Id.* Ms. Tracy testified that the ER physician told her that R.S. "just d[id not] feel good. She's tired, so that's why she[is] not moving." Tr. 24:19–20. Ms. Tracy wrote that she slept next to R.S.'s crib that night, because at that point, "R.S. was not moving." Pet'r's Ex. 1 ¶ 34.

She averred that "[a]t about 4 am the following morning, R.S. woke up[,] tried to nurse, but could not hold up her head to do so. Her eyes were open[,] but she seemed non[-]responsive." *Id.* ¶ 35. Ms. Tracy noted that she and her husband then took R.S. to a different hospital in Colorado Springs, where R.S. underwent cervical spine and brain MRIs and a lumbar puncture "to rule out central nervous system pathology." *Id.* ¶¶ 35–38. During her testimony, Ms. Tracy clarified that R.S. was admitted and this testing occurred on April 2, 2013; R.S.'s TM diagnosis was made the same day. Tr. 26:10–25. By April 4, 2013, R.S. could not hold herself up or move her arms and legs. Tr. 28:15–25, 29:1–2. She wrote that R.S. received "five days of high dose intravenous steroids and received one IVIG treatment[]" for clinical indications of weakness and TM. Pet'r's Ex. 1 ¶¶ 38–39. Ms. Tracy indicated that R.S. has received treatment for her TM throughout 2013 and thereafter, including the placement of a CVC line, plasmapheresis ("PLEX") treatments, inpatient rehabilitation, and outpatient PT and OT. *Id.* ¶¶ 40, 42–46, 49. She also noted that R.S.'s treating neurologist is Dr. Teri Schreiner. *Id.* ¶ 47. Ms. Tracy documented R.S.'s pre and post vaccination condition with photographs, which she also discussed during her testimony. *Id.* ¶ 29; *see also* Tr. 18–30.

Ms. Tracy described R.S.'s condition as of January of 2016 and noted that R.S.'s "condition has improved, but she remains disabled. Her primary issues relate to mobility and other medical consequences . . . ." *Id.* ¶ 50. She wrote that R.S. receives three outpatient PT sessions per week and two outpatient OT sessions per month. *Id.* ¶ 51. Ms. Tracy averred that R.S. "is able to walk with the assistance of a walker and has recently begun working on transitioning to forearm crutches." *Id.* She wrote that R.S. "suffers from spasticity and tone in her legs and receives regular Botox injections every [ninety] days to help relieve that tightness." *Id.* Ms. Tracy noted that these difficulties "with getting [R.S.'s] legs completely straight[make p]otty training [] an issue[.]" *Id.* She indicated that R.S. sees a urologist and pediatric pelvic floor specialist to assist with her ongoing bladder issues. *Id.*; *see also* Tr. 35:20–21. She further wrote that R.S. attends school and "tries her best to keep up with kids her age[] but is forced to rely on the help of her teachers and aides for outdoor activities." Pet'r's Ex. 1 ¶ 51. Ms. Tracy testified that they keep a wheelchair at school, "for fire drills and things like that." Tr. 35:14–19.

Ms. Tracy noted that Dr. Schreiner told her not to vaccinate R.S. with any live vaccines. Tr. 43:17–19; Pet'r's Ex. 1 ¶ 44. On cross-examination, Ms. Tracy testified that she did not recall R.S.'s treaters telling her that the cause of R.S.'s TM was idiopathic or post-infectious. Tr. 41–42. Under my questioning, Ms. Tracy explained that R.S.'s pulmonary and respiratory issues, such as her asthma and tendency for bronchitis resolved when R.S. was five years old. Tr. 42:19–25, 43:1–9. On re-direct, Ms. Tracy stated that immediately after R.S. developed TM, her respiratory issues

became more difficult to deal with because she had decreased diaphragm strength from the TM. Tr. 44:21–25, 45:12–14.

Petitioners' second affidavit was authored by Mr. Danny Stotler, R.S.'s father. Pet'r's Ex. 2 ¶¶ 1–2. Mr. Stotler's affidavit is essentially identical to Ms. Tracy's affidavit and a recitation of its contents is unnecessary. *See id.* ¶¶ 3–33; *see also* Pet'r's Ex. 1.

III. Experts

A. Expert Review

1. Petitioners' Expert, Teri Schreiner, M.D.

Dr. Schreiner received her medical degree from the University of Rochester in 2006. Pet'r's Ex. 69 at 1, ECF No. 61-1. She completed a residency in pediatrics at the University of Colorado in 2008. *Id.* She also completed residencies in neurology and child neurology at the same institution in 2009 and 2011, respectively. *Id.* Dr. Schreiner held academic appointments in neuro-immunology at the University of Colorado from 2011 to 2017. *Id.* She currently serves as an Associate Professor of Neurology at the University of Colorado. *Id.* She is board-certified in psychiatry and neurology with special qualifications in child neurology. *Id.* at 2. Dr. Schreiner's qualifications as a pediatric neuro-immunologist include, in part, her clinical experience treating children with immune-mediated demyelinating conditions such as TM, presenting on the biology of such conditions, and publishing extensively on disorders of the spinal cord, as well as neurologic complications of vaccinations, specifically. *See id.* at 2–12; *see also* Pet'r's Ex. 71 at 1–2. She is also "one of a small group of pediatric neuroimmunologists in the country that specialize in pediatric demyelinating disorders." Pet'r's Ex. 71 at 1. Much of Dr. Schreiner's research and publications specifically involves disorders of the spinal cord. *Id.*

2. Petitioners' Expert, Lawrence Steinman, M.D.

Dr. Steinman received his medical degree from Harvard University in 1973. Pet'r's Ex. 23 at 1. He completed his post-graduate training at Stanford University, where he completed an internship in surgery in 1973, a residency in pediatrics in 1974, and a residency in pediatric and adult neurology from 1977 to 1980. *Id.* He became board-certified in neurology in 1984. *Id.* at 2. He served as the Chairman of the Immunology Program at Stanford for approximately ten years from 2002 to 2011. *Id.* at 1. He currently serves as a Professor of Neurology, Pediatrics, and Genetics at Stanford University's Department of Neurology and Neurological Sciences. *Id.* Dr. Steinman's curriculum vitae includes over five-hundred and forty published articles of which he is a listed author. *See id.* at 5–45.

During the hearing, he noted he "did residency training in pediatrics and neurology." Tr. 47:16–17. He explained that the focus of his medical research is on "how the immune system attacks the nervous system in diseases like multiple sclerosis, like [TM], and like some of the inflammatory neuropathies." Tr. 48:11–14. Dr. Steinman testified that his current clinical practice involves "treat[ing] patients with [TM,]" including children and infants. Tr. 48:15–19. He stated that he has testified many times in the Vaccine Program. Tr. 119–120.

Dr. Steinman submitted three expert reports and testified during the first part of the entitlement hearing. *See* Pet'r's Exs. 22, 46, 60; Tr. 46–107. Following the break in proceedings, Dr. Steinman submitted two additional expert reports and subsequently testified during the second part of the entitlement hearing. Pet'r's Exs. 97, 101; Tr. 118–128, 187–194. Petitioners did not offer Dr. Steinman as an expert during either part of the hearing. I believe this was an oversight. However, he has been recognized as an expert in neurology in numerous Program cases before me, as well as other special masters. Therefore, I will *sua sponte* recognize him as such.

3. Respondent's Expert, Stephen McGeady, M.D.

Dr. McGeady received his medical degree from Creighton University in Omaha, Nebraska in 1967. Resp't's Ex. B at 1. From there, Dr. McGeady was in the 1st Infantry of the U.S. Army in Vietnam from 1968–1969 and was then employed at the Fitzsimons Army Hospital in Denver, CO from 1969–1970. *Id.* Dr. McGeady completed a residency in pediatrics at St. Christopher's Hospital in Philadelphia, PA in 1972. *Id.* He also completed a fellowship in psychiatry and allergy at Duke University in Durham, NC in 1974. *Id.* Dr. McGeady has been the Emeritus Chief of the Allergy, Asthma, and Immunology Division at duPont Hospital for Children in Wilmington, DE since 2007. *Id.* He has also served as a Professor of Pediatrics at Jefferson Medical College in Philadelphia since 2005. *Id*. Dr. McGeady is board-certified in pediatrics and allergy and immunology. *Id.* He has received numerous honors, and he holds memberships in several professional and scientific societies. *Id.* at 2. His curriculum vitae lists over two-hundred and sixty publications, including articles, abstracts, book chapters, and editorials of which he is a listed author. *See id.* at 2–14.

During the hearing, Dr. McGeady explained that as part of his clinical practice, he supervises fellows in allergy and immunology. Tr. 130:23–25. He also interacts with medical students "as part of their pediatrics rotation." Tr. 131:13–16. Dr. McGeady noted that he has "had exposure to" patients with TM, but he personally has not been "involved in direct care of those patients." Tr. 132:23–25, 133:1–5. Instead, he noted that he has "supervised people who cared for them directly." Tr. 133:5–6. Dr. McGeady testified that since he is not a neurologist, it "would not be expected" for him to provide treatment to patients with TM. Tr. 133:11–17. He explained that his testimony is instead limited to "the immunology of Petitioner[s'] theory of causation[.]" Tr. 133:18–20. Dr. McGeady noted that he has testified approximately thirty times in the Vaccine Program. Tr. 134:1–3.

Dr. McGeady submitted three expert reports prior to the first entitlement hearing, and he did not testify during the first part of the hearing as a result of Petitioners' new theory of causation. *See* Resp't's Exs. A, K, T. Following the break in proceedings, Dr. McGeady submitted two additional reports, and subsequently testified during the second part of the hearing. Resp't's Exs. JJ, MM; Tr. 129–185. Respondent offered Dr. McGeady as an expert in pediatric immunology, pediatric clinical allergy/immunology, and pediatrics without objection, and I recognized him as such. Tr. 134:20–25, 135:1–7.

B. Expert Reports and Testimony

1. Petitioners' Expert, Dr. Schreiner

Dr. Teri Schreiner, R.S.'s treating neurologist, submitted a letter in support of Petitioners' claim, and she did not testify at the entitlement hearing. Pet'r's Ex. 71. She wrote that she has been R.S.'s primary treating neurologist and "has been involved in her care since her presentation in April[of] 2013." *Id.* at 1. Dr. Schreiner thoroughly described her extensive qualifications in pediatric demyelinating diseases and opined that "it is more likely than not that the immunizations that [R.S.] received on March 18, 2013[,] were responsible for the immune response causing the inflammation in her spinal cord." *Id.* at 1–2. She wrote that "there is sufficient biologic evidence (to be further detailed by Dr. Steinman) and circumstantial evidence to support this link." *Id.* at 3.

She wrote that since 2013, she has seen R.S. "regularly to monitor her progress." *Id.* at 2. Dr. Schreiner indicated that she saw R.S. most recently on August 14, 2019. *Id.* She described R.S.'s condition consistent with the medical records from this visit, noting that R.S. "was able to walk with bilateral walking aids. She had a wide-based [gait] with a pelvic tilt and [exhibited a] flinging motion of her legs . . . toe-dragging . . . [and] impaired sensation to vibration bilaterally." *Id.* She continued that as a result, R.S. has difficulty ambulating, is at risk for falls, and will "continue to require equipment (ankle braces, walking aides, etc.)[,] procedures (orthopedic surgeries and [B]otox for spasticity)[,]" and PT. *Id.*

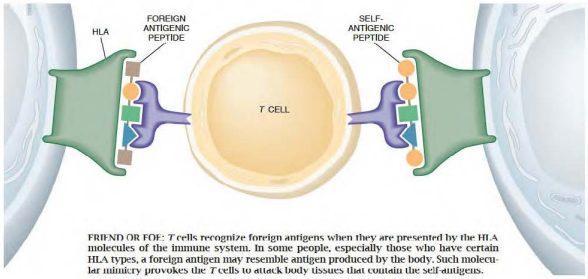
Regarding causation, Dr. Schreiner opined as to the mechanism by which a vaccine causes TM. *Id.* She noted that "[o]ne of the most plausible explanations is molecular mimicry." *Id.* Dr. Schreiner explained that molecular mimicry "describes a process whereby a person is vaccinated against a disease. The person['s] immune system is 'trained' to fight that disease. However, the immune system confuses the signatures and fights a similar-appearing *self*-protein." *Id.* (emphasis in original). She continued that "[i]n the case of [TM], this is a protein in the spinal cord. The inflammatory attack on the spinal cord damages the axons that transmit signals from the brain to the body and sensations from the body to the brain." *Id.*

Dr. Schreiner discussed the time between R.S.'s vaccination and the onset of her TM. *Id.* She wrote that "the timing of [TM two] weeks after vaccination would be consistent with an immune-mediated attack as a result of vaccination." *Id.* Dr. Schreiner also addressed potential alternative causes for R.S.'s TM, such as infections and autoimmune diseases, and noted that the testing for alternative causes of TM were negative. *Id.* She elaborated that R.S. did not have any "known illnesses prior to the onset of [TM] to suggest an infectious trigger[]" and "[o]ver the [five] years that [she] has cared for [R.S.], she has not developed any systemic signs of lupus or other autoimmune disorder to implicate this as the cause of [R.S.'s TM]." *Id.*

2. Petitioners' Expert, Dr. Steinman

Dr. Steinman submitted five expert reports and testified during the hearing. *See* Pet'r's Exs. 22, 46, 60, 97, 101; Tr. 46–107, 118–128, 187–194. In his first expert report, Dr. Steinman concluded that R.S.'s "Prevnar 13 vaccine, by a preponderance of evidence, triggered [TM] in [R.S.]." Pet'r's Ex. 22 at 12. Dr. Steinman explained that this is possible because of the concept of molecular mimicry. *Id.* at 5. He relied on a diagram,[39] which "describes how shared structures on a virus or bacteria or in a vaccine can trigger a cross-reactive response to [it]self[:]"

[39] L. Steinman, *Autoimmune Disease,* 269 SCIENTIFIC AMERICAN 106–14 (1993).



Id. (citing Pet'r's Ex. 34, ECF No. 25-4). The diagram depicts how "T cells recognize foreign antigens when they are presented by the HLA molecules of the immune system." Pet'r's Ex. 34 at 4. Dr. Steinman noted that "[i]n some people, especially those who have certain HLA types, a foreign antigen may resemble antigen[s] produced by the body." *Id.* He concluded that "[s]uch molecular mimicry provokes the T cells to attack body tissues that contain the self-antigens." *Id.* Dr. Steinman continued that "[i]n autoimmune diseases, the immune system . . . mistakenly attacks the body's own tissue, causing inflammation and, in some cases, damage to myelin within the spinal cord." Pet'r's Ex. 22 at 7. Based on this, he noted that "some scientists suggest that [TM] may also be an autoimmune disorder." *Id.* Dr. Steinman testified that 'autoimmune' and 'immune-mediated' mean the same thing. Tr. 52:15–20.

He vehemently dismissed Dr. McGeady's criticisms of his molecular mimicry theory, noting that he "shall not debate whether molecular mimicry is a viable theory." Pet'r's Ex. 46 at 1. He wrote that he has "written about this [theory] in numerous peer reviewed publications . . . testified about [it] in over twenty cases before this [C]ourt . . . [and i]n many cases[,] . . . prevailed[.]" *Id*.

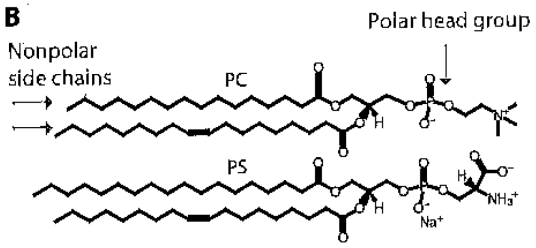
Dr. Steinman described molecular mimicry in the context of an inflammatory condition of peripheral nerves, Guillain-Barré syndrome ("GBS").[40] Pet'r's Ex. 22 at 7. He wrote that "phospholipids are seen in [GBS]." *Id*. He explained that "phospholipids are components of the myelin sheath in humans, and that they are targeted by antibodies in neuroinflammation in the central nervous system[.]" *Id.* (citing Pet'r's Exs. 37, 38, ECF No. 25-5).[41] He relied on an article by Gilburd et al.,[42] in which the authors found that '"sixteen [GBS] sera were studied for the presence of antibodies to . . . phosphatidyl-ethnolamine, phosphatidyl-choline, phosphatidylserine

[40] Guillain-Barré Syndrome ("GBS") is "rapidly progressive ascending motor neuron paralysis of unknown etiology, frequently seen after an enteric or respiratory infection. An autoimmune mechanism following viral infection has been postulated. It begins with paresthesias of the feet, followed by flaccid paralysis of the entire lower limbs, ascending to the trunk, upper limbs, and face; other characteristics include slight fever, bulbar palsy, absent or lessened tendon reflexes, and increased protein in the cerebrospinal fluid without a corresponding increase in cells. Variant forms include acute autonomic neuropathy, Miller-Fisher syndrome, acute motor axonal neuropathy, and acute motor-sensory axonal neuropathy." *Dorland's* at 1832.

[41] J. Kanter, et al., *Lipid Microarrays Identify Key Mediators of Autoimmune Brain Inflammation,* 12:1 NATURE MEDICINE 138–43 (2006); P. Ho, et. al., *Identification of Naturally Occurring Fatty Acids of the Myelin Sheath that Resolve Neuroinflammation,* 4 SCIENCE TRANSLATION MEDICINE 137–52 (2012).

[42] B. Gilburd, et al., *Autoantibodies to Phospholipids and Brain Extract in Patients with the Guillain-Barré Syndrome: Cross-Reactive or Pathogenic?,* 16:1 AUTOIMMUNITY 23–27 (1993).

. . . [s]ix of the [sixteen] GBS sera had autoantibodies to one or more of the antigens studied."' Pet'r's Ex. 22 at 7 (citing Pet'r's Ex. 39, ECF No. 25-5). He further relied on an article by Ho et al.[43] to note that "[l]ipids constitute 70% of the myelin sheath, and autoantibodies against lipids may contribute to the demyelination that characterizes multiple sclerosis ("MS")." Pet'r's Ex. 22 at 7 (citing Pet'r's Ex. 38 at 1). The authors of the Ho et al.[44] article, including Dr. Steinman, described an animal model of MS they used to "explore the role of identified lipids in autoimmune demyelination." *See id.* Dr. Steinman wrote that the authors "found that autoantibodies in MS target a phosphate group in phosphatidylserine and oxidized phosphatidylcholine derivatives." Pet'r's Ex. 22 at 7; *see also* Pet'r's Ex. 38 at 1. He cited a diagram used in the Ho et al.[45] article, which shows the "structure of phosphatidyl choline, phosphatidylserine[,] and the common location of the polar head groups targeted by antibodies[:]"



Pet'r's Ex. 22 at 8 (citing Pet'r's Ex. 38 at 4). Based on the articles by Ho et al. and Gilburd et al., Dr. Steinman concluded that in diseases involving inflammation of the central nervous system ("CNS"), as well as in inflammation of the peripheral nervous system, "there is evidence of an antibody response to phosphotidyl [sic] choline structures." Pet'r's Ex. 22 at 8. Dr. Steinman then opined that phospholipids are contained in the Prevnar 13 vaccine. *Id.* Based on this, he concluded that it would "[t]hus [] be logical [] that a vaccine like Prevnar 13 would immunize the recipient against this [phosphorylcholine] component of pneumococcus. And immunity to this phospholipid [] is involved in neuroinflammation in both the central and peripheral nervous system." Pet'r's Ex. 22 at 8.

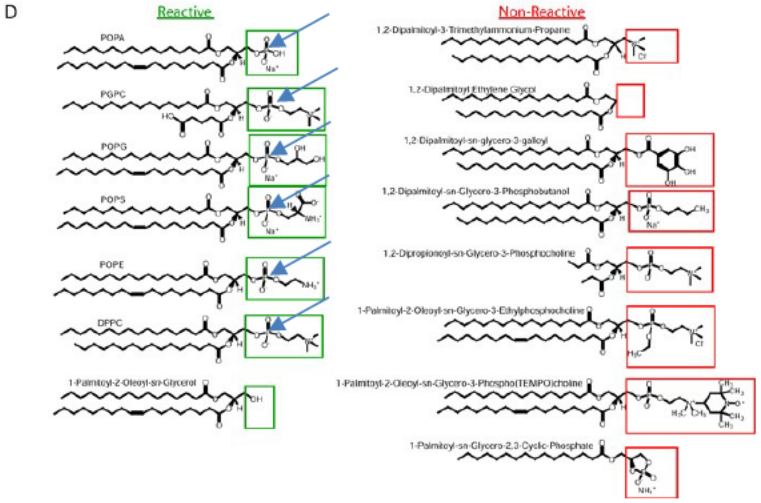
He discussed in detail his focus on the phospholipids contained in the PCV 13 vaccine, as well as Dr. McGeady's criticism that the vaccine does not contain phospholipids. Pet'r's Ex. 22 at 8; Pet'r's Ex. 46; Pet'r's Ex. 60. At the entitlement hearing held in January of 2020, Dr. Steinman conceded this point, and agreed that Dr. McGeady was correct in his assertion that the PCV 13 vaccine does not contain phospholipids. Tr. 61:6–9. Dr. Steinman altered his theory so that he no longer relied on the presence of phospholipids in the Prevnar 13 vaccine. *See* Tr. 57:11–58:10. Dr. Steinman clarified that he made a mistake in referring to phospholipids within his written reports. Tr. 57:14–18 (citing Pet'r's Exs. 22, 46, 60). He explained that he altered his theory on the stand because he wanted to "help the Court get it right." Tr. 79:15. This mistake in nomenclature prompted Dr. Steinman to alter his theory and focus on the sugars (polysaccharides) in the vaccine, rather than the fatty acids (phospholipids). Tr. 57:11–25, 58:1–3, 63:11–16. He testified that instead of phospholipids, he "should have used the term 'phosphoglycerol' and called them

[43] P. Ho, et. al., *Identification of Naturally Occurring Fatty Acids of the Myelin Sheath that Resolve Neuroinflammation,* 4 SCIENCE TRANSLATION MEDICINE 137–52 (2012).
[44] *See* Ho, et. al., *supra* note 43.
[45] *See id.*

'phospho polysaccharides.'" Tr. 57:15–18. Dr. Steinman emphasized that the phosphoglycerol is the target, not the phospholipid. Tr. 61:3–6. He maintained that the attack is still on the phospho element of the molecule and Petitioners' theory of causation does not change depending on whether or not the molecule is a sugar or a fatty acid. Tr. 67:1–13, 69:21–25, 70:1–3. While this case ultimately involves saccharides, Dr. Steinman incorporated many of his same arguments that he originally posited regarding lipids. Dr. Steinman explained that his theory is therefore that "the immune response to the phosphoglycerol or phosphocholine molecule in the Prevnar 13 vaccine cross-reacts with the phosphoglycerate or phosphocholine head – polar head group in the components of the myelin sheath[.]" Tr. 95:5–10.

Dr. Steinman relied on the similarities between cases of MS and TM and opined that the phosphoglycerols attached to polysaccharides in the PCV 13 vaccine, cross-react with the phosphoglycerols attached to the phospholipids in the spinal cord to cause TM. Tr. 60:16–61:14. To support his position, Dr. Steinman focused on the article by Ho et al.,[46] wherein the authors isolated the components and asked, "are there any structural features that allow us to see what the [more] specific point of attack of the immune system was." Tr. 56:22–25. He testified that they found that the "point of attack" was a "phosphate group in a chemical structure that links these complex molecules together . . . called glycerol." Tr. 57:1–4. Specifically, the authors found that the antibodies were "directly targeting the . . . phosphate glycerol polar group" in six out of seven cases:

The arrows represent the point of attack on the phosphate polar head group of phosphoglycerol, as seen in six out of seven cases.



Tr. 60:1–19. Dr. Steinman broke it down even more and stated that "[i]t[is] the phosphate on the glycerol, so it's targeting the phospho of the phosphoglycerol[]" in patients with MS. Pet'r's Ex. 97 at 6; Tr. 60:19–20. Dr. Steinman's theory therefore focused on the phosphoglycerols in the Prevnar 13 vaccine, independent of whether they are attached to a lipid, as seen in the case of MS, or a saccharide carrier, like in the Prevnar 13 vaccine. *See* Tr. 67:1–13, 69:21–25, 70:1–3. Dr. Steinman wrote that he "*did specify* which epitope is shared by the CNS and the phosphoglycerol molecule." Pet'r's Ex. 97 at 2 (emphasis in original). He elaborated on this and noted that the immune system is making an antibody to either the saccharide attached to the Prevnar 13 vaccine or the lipid in MS patients; the attack is still on the phosphate group. Pet'r's Ex. 97 at 2–3 (citing Tr. 89:4–15, 90:1–7).

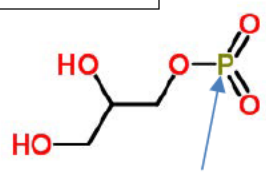
[46] *See* Ho, et. al., *supra* note 43.

Dr. Steinman explained why he compared MS with TM. Tr. 103:3–23. He stated that they are both neuroinflammatory conditions of the CNS and "both can involve the spinal cord." Tr. 103:12–13. He explained that "[t]he difference is that MS is a chronic life-long disease that relapses and remits." Tr. 103:15–16. Whereas TM "is most often . . . a one-time only disease." Tr. 103:16–18. Dr. Steinman indicated that "one very important distinguishing criteria [sic]" for diagnosis is the longevity of the disease. Tr. 103:19–23. He continued that MS is often misdiagnosed as TM because "[w]hen it recurs, a person can say, 'oh, the first attack of [TM] was just the beginning of [] MS.'" Tr. 103:24–25, 104:1–3. Dr. Steinman noted that "[y]ou really can[not]" diagnose TM as distinct from MS prior to a relapse of TM. Tr. 104:23–25.

Dr. Steinman acknowledged on cross-examination that the Ho et al.[47] article does not discuss TM, but rather MS. Tr. 122:10–20. However, on rebuttal, Dr. Steinman noted that while the authors discussed MS, they also discuss phosphoglycerol, which is listed in the U.S. patent for the Prevnar 13 vaccine.[48] Tr. 190:4–11 (citing Pet'r's Exs. 38, 96). Dr. Steinman disagreed with Dr. McGeady's contention that "phosphoglycerol is too small[]" to be immunogenic and that it changes formation "depending on what[is] attached to the phosphoglycerol." Tr. 190:17–21. Dr. Steinman stated that he has not "seen any data to support that," but he noted that the Ho et al.[49] article "refutes that." Tr. 190:21–23 (citing Pet'r's Ex. 38). He explained that "it does[not] matter what the phosphoglycerol is attached to if they're lipids. They could have long-chain fatty acids, short-chain fatty acids. The immune system still, like a laser, hits the phosphoglycerol." Tr. 190:24–25, 191:1–3.

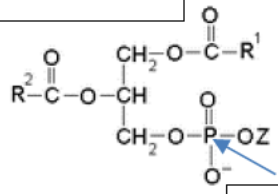
He further relied on the U.S. patent for the Prevnar 13 vaccine[50] and noted that it "refers to the glycerol phosphate more than a dozen times[.]" Tr. 94:1–3 (citing Pet'r's Ex. 96). Dr. Steinman opined that it is "the lipids [] in the myelin sheath[that are] attacked through th[e] same phosphate head group on phosphoglycerol or on phosphocholine." Tr. 96:1–7. He based his opinion on the "shared structure and what[is] known about how the immune system attacks the components of the Prevnar [13] vaccine, and how [the immune system attacks the components of the myelin sheath] in a human disease somewhat related to [TM] known as [MS.]" Tr. 96:1–7. Dr. Steinman explained that this is possible because the glycerol phosphate in the polysaccharide of the Prevnar 13 vaccine is "identical" to the glycerol phosphate "that was the focus of the immune attack in MS when [the] glycerol phosphate was holding it on to the lipid." Tr. 90:25, 91:1–2; *see also* Pet'r's Ex. 60 at 2–3. Dr. Steinman provided diagrams of the molecular structures of phosphoglycerol and glycerophospholipids:

Phosphoglycerol



Polar head group

Glycerophospholipid



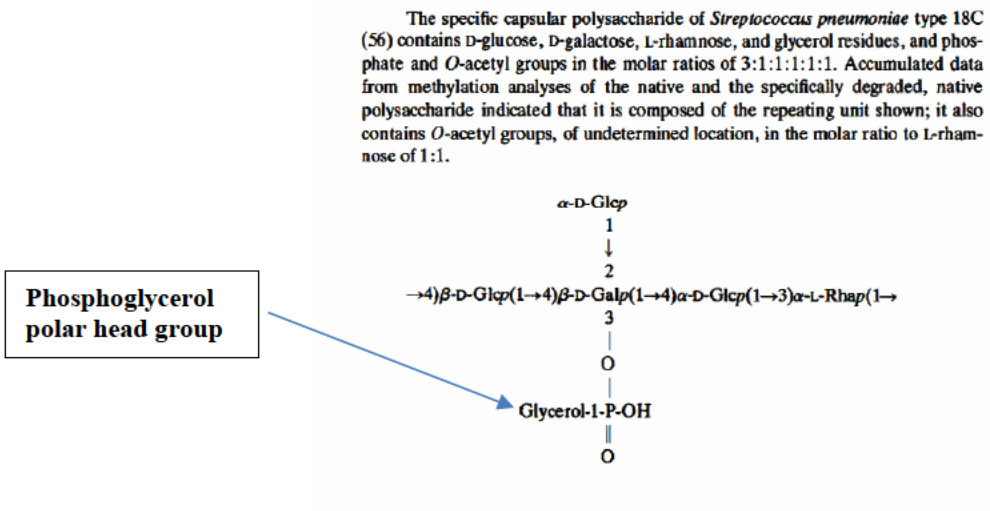
Polar head group

[47] *See* Ho, et. al., *supra* note 43.
[48] U.S. Patent No. 9,492,559 B2 (filed Nov. 15, 2016).
[49] *See* Ho, et. al., *supra* note 43.
[50] *See* U.S. Patent, *supra* note 48.

Pet'r's Ex. 60 at 2–3.

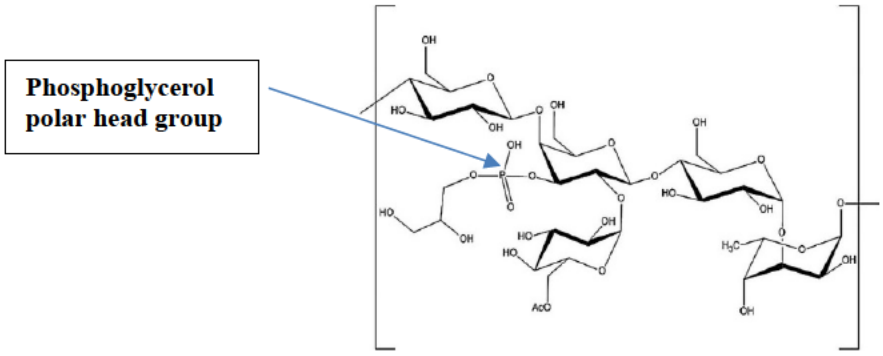
Regarding the Prevnar 13 vaccine specifically, Dr. Steinman explained that in the vaccine, "it[is] the sugars of the pneumococcus coupled to this phosphoglycerol." Tr. 62:15–17. Dr. Steinman relied on the package insert[51] for the Prevnar 13 vaccine that noted that "[t]he pneumococcal 13-valent conjugate vaccine is a sterile suspension of the capsular polysaccharide antigens of *Streptococcus pneumoniae* ["s. pneumoniae"] serotypes 1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, and 23F individually conjugated by reductive amination to the non-toxic diphtheria CRM197 protein." Pet'r's Ex. 35 at 1, ECF No. 25-4. Based on this, Dr. Steinman maintained that "it is unmistakably clear that the Prevnar 13 [vaccine] contains 'capsular polysaccharide antigens of *Streptococcus pneumonia.*'" Pet'r's Ex. 46 at 2 (citing Pet'r's 35 at 1).

He also relied on the Lugowski et al.[52] article to note that "there is explicitly . . . a phosphoglycerol attached to a galactoside in the 18C pneumococcal sugar." Tr. 62:19–23 (citing Pet'r's Ex. 53, ECF No. 30-8). The Lugowski et al. article contains a description and diagram of the molecular structure of the streptococcus pneumoniae serotype 18C "written in words." Pet'r's Ex. 53 at 1; Tr. 90:14–16. It indicates that there is a phosphorous containing molecule in the streptococcus pneumoniae polysaccharide capsule of serotype 18C, which is contained in the current pneumococcal vaccine:



Pet'r's Ex. 53 at 2. Dr. Steinman further relied on the diagram contained in the Chang et al.[53] article, which, without words, shows "the [same] capsular polysaccharide in streptococcus pneumonia serotype 18C[:]"

[51] *Prevnar-13 Package Insert,* FOOD & DRUG ADMINISTRATION (https://www.fda.gov/vaccines-blood-biologics/vaccines/prevnar-13).
[52] C. Lugowski & H. Jennings, *Structural Determination of the Capsular Polysaccharide of Streptococcus Pneumoniae Type 18C,* 131 CARBOHYDRATE RES. 119–29 (1984).
[53] J. Chang, et al., *Relevance of O-acetyl and Phosphoglycerol Groups for the Antigenicity of Streptococcus pneumoniae Serotype 18C Capsular Polysaccharide,* 30 VACCINE 7090–96 (2012).



Tr. 88:9–18 (citing Pet'r's Ex. 52 at 2). He used the diagram to point out the phosphate group, which serves as "part of the anchor to the [] phosphoglycerol component." Tr. 88:17–22. He stated that without that, "18C would have no immunogenicity." Tr. 88:24–25. The authors of the Chang et al. article found that "[t]he loss of these [phospho polar head] groups may potentially reduce the ability of the 18C polysaccharide to induce the desired immune response." Pet'r's Ex. 52 at 1. The authors concluded that "[t]he linkage is a central component of the 18C polysaccharide structure" and the "glycerol phosphate [group] must be preserved for conserving adequate antigenicity of the 18C capsular polysaccharide[]" contained in the PCV 13 vaccine. *Id.* Dr. Steinman opined that "[i]t is doubtful that the preparatory procedures for purifying 18C capsular polysaccharide[s] would destroy covalent linkages." Pet'r's Ex. 46 at 4. As support, he noted that "removal of the covalent chemical linkage of the phosphate group would be unlikely because it would reduce the immunogenicity of the vaccine itself." *Id.* at 5 (citing Pet'r's Ex. 52).

Dr. Steinman then relied on the Chuang et al.[54] article, which "describe[s] a phosphate choline in the polar group in the serotype 19A of the streptococcus pneumonia bacteria." Tr. 93:2–5 (citing Pet'r's Ex. 40 at 1, ECF No. 25-5). Dr. Steinman testified that the importance of the phosphocholine molecule to streptococcus pneumonia serotype 19A is that its presence "increases the severity of the pneumonia that pneumococcus can cause." Tr. 93:16–22. The authors of the Chuang et al. article found that the phosphorylcholine polar head group in serotype 19A of s. pneumoniae is critical to the success of the infection in serotype 19A. Pet'r's Ex. 40 at 1. Dr. Steinman explained that this means an effective vaccine against serotype 19A must also generate an immune response to that head group. Tr. 93:19–24. He concluded, using these articles as support, that if there is "no phosphoglycerol, [there would be] no good immune response, even to the polysaccharides[]" because the attack is on that phospho polar head group. Tr. 191:5–9. He explained that if "[y]ou take [the phosphoglycerol] away, you lose the immunogenicity." Tr. 58:13–14. He maintained based on the medical literature that the phosphoglycerol "is the vital connection to keep in the vaccines. If it[is] taken away . . . it loses immunogenicity[,]" and "of course, you want a vaccine to be immunogenic." Tr. 58:6–13, 61:10–14, 63:6–7 (citing Pet'r's Exs. 40, 52, 53).[55]

---

[54] Y. Chuang, et al., *Impact of the glpQ2 Gene on Virulence in a Streptococcus pneumoniae Serotype 19A Sequence Type 320 Strain,* 83 INFECTION & IMMUNITY 682–92 (2015).

[55] Y. Chuang, et al., *Impact of the glpQ2 Gene on Virulence in a Streptococcus pneumoniae Serotype 19A Sequence Type 320 Strain,* 83 INFECTION & IMMUNITY 682–92 (2015); J. Chang, et al., *Relevance of O-acetyl and Phosphoglycerol Groups for the Antigenicity of Streptococcus pneumoniae Serotype 18C Capsular Polysaccharide,* 30 VACCINE 7090–96 (2012); C. Lugowski & H. Jennings, *Structural*

Dr. Steinman noted that "the antibody arm of the immune system precisely recognizes small structures[]" such as "the 'small' phosphate polar head group that is present in the CNS." Pet'r's Ex. 101 at 4. Since the same phosphate polar head group is also present in Prevnar 13, this fact "strongly suggests that it could trigger a cross-reactive immune response to the CNS[.]" *Id.* He maintained that "[t]his theory therefore describes how components of Prevnar 13 can elicit cross-immunity to components of the myelin sheath that are known to be targeted in inflammation in the central nervous system resulting in [TM]." Pet'r's Ex. 22 at 9.

Dr. Steinman further addressed the points raised in Dr. McGeady's report and noted that Dr. McGeady presumed the wrong polysaccharide in the Prevnar 13 vaccine. Pet'r's Ex. 97 at 3. Dr. Steinman wrote that the large carrier molecule in the Prevnar 13 vaccine is not the polysaccharide capsule of one or two pneumococcal serotypes, it is the diphtheria CRM protein. *Id.* He relied on the package insert[56] for Prevnar 13 to support this conclusion. *Id.* (citing Pet'r's Ex. 35 at 25). Dr. Steinman also relied on the e-mail response he received from the Center for Disease Control ("CDC"), which "clearly state[d] that the [d]iphtheria CRM protein is the carrier[]" protein. Pet'r's Ex. 97 at 4–5; *see also* Pet'r's Ex. 60 at 4.

He then responded to Dr. McGeady's assertion that "the immune system produc[ing] antibod[ies] promiscuously to molecules such as phosphoglycerol regardless of their molecular position[] ignore[d] the complexity of antibody production . . . ." Pet'r's Ex. 101 at 1. He continued that "[t]he precision of antibodies is exquisite and the phosphate polar head group on the glycerol was targeted regardless of what its attachments were." *Id.* at 2 (citing Pet'r's Ex. 38). Dr. Steinman noted that his opinion relied on "actual experimental evidence presented in an outstanding peer reviewed journal, not on generalities about the 'promiscuity' of antibody antigen interaction." *See id*. Dr. Steinman opined that Dr. McGeady "engage[d] in generalities about the immune system and its specificities[.]" Pet'r's Ex. 101 at 1. He relied on an article by Pinto et al.,[57] to demonstrate the specificity of antibodies to even small sugars. Pet'r's Ex. 97 at 8 (citing Pet'r's Ex. 100, ECF No. 95-5). The authors analyzed the neutralizing antibody to the spike protein in SARS CoV-2 and noted that it "actually binds a sugar, called fucose, on the spike protein." Pet'r's Ex. 97 at 6 (citing Pet'r's Ex. 100 at 7). They found that the antibody binding regions, called complementarity determining regions ("CDRs"), "sandwich the SARS-CoV-2 glycan . . . through contacts with the core fucose moiety[.]" Pet'r's Ex. 100 at 3. Dr. Steinman explained that "[s]mall molecules are targeted by the immune system when they are conjugated to a carrier. In MS, the carriers [] are the myelin proteins." Pet'r's Ex. 97 at 6 (citing Pet'r's Ex. 38); Tr. 57:9–10, 60:7–20. He continued that "[i]t is known that the surface area of [an antibody] has only a small portion of the antibody surface that contacts a small portion of the antigen." Pet'r's Ex. 97 at 6. Based on this, Dr. Steinman wrote that "the capacity of an antibody to bind a small sugar or a small molecule like phosphoglycerol is not unusual." *Id.*

Dr. Steinman discussed Dr. McGeady's assertion that TM is more suggestive of a cell-mediated damage than it is of an antibody-mediated injury. Pet'r's Ex. 60 at 6. He wrote that "Dr.

Determination of the Capsular Polysaccharide of Streptococcus Pneumoniae Type 18C, 131 CARBOHYDRATE RES. 119–29 (1984).

[56] *See Prevnar-13 Package Insert, supra* note 51.

[57] D. Pinto, et al., *Cross-neutralization of SARS-CoV-2 by a Human Monoclonal SARS-CoV Antibody,* NATURE https://doi.org/10.1038/s41586-020-2349-y (2020).

McGeady is incorrect on this." *Id.* He testified that "[TM] is never just cell-mediated, nor is it ever just antibody-mediated." Tr. 188:2–4. Dr. Steinman explained that an "[a]ntibody mediated injury is a cornerstone of our understanding of [TM]." Pet'r's Ex. 60 at 6. He relied on an article by Kaneko et al.,[58] to highlight that TM "is driven by antibodies to either [aquaporin 4 ("AQP4")] or to myelin oligodendrocyte glycoprotein [("MOG")]." *Id.* (citing Pet'r's Ex. 65 at 1, ECF No. 45-7). The authors noted that "[w]hether MOG-IgG is pathogenic and directly involved in the pathogenesis is not fully understood, but some recent studies support MOG-IgG's pathogenicity." *See id.* They continued, "[f]or example, MOG-IgG can induce alteration of oligodendrocyte cytoskeleton organization in vitro . . . biopsied cases showed there were depositions of IgG and complements associated with demyelination in the lesions of cases with MOG-IgG+ disease[.]" Pet'r's Ex. 65. Dr. Steinman wrote that this "is consistent with the MS pattern II pathology and suggests a pathogenic role for humoral immunity in the lesion formation." Pet'r's Ex. 60 at 6.

Dr. Steinman applied his theory to the facts of R.S.'s case. Pet'r's Ex. 22 at 6. He again cited the package insert[59] for the Prevnar 13 vaccine and reiterated its contents, including saccharides of capsular antigens of s. pneumoniae serotypes 18C and 19A. *Id.* (citing Pet'r's Ex. 35 at 1). He noted that to manufacture the vaccine, "[t]he individual polysaccharides are purified through centrifugation, precipitation, ultrafiltration, and column chromatography. The polysaccharides are chemically activated to make saccharides, which are directly conjugated by reductive amination to the protein carrier CRM197, to form the glycoconjugate." *See id.* The package insert explains that "[t]he individual glycoconjugates are compounded to formulate Prevnar 13." *See* Pet'r's Ex. 35. It continues that "[p]otency of the formulated vaccine is determined by quantification of each of the saccharide antigens and by the saccharide to protein ratios in the individual glycoconjugates." *Id.*

He relied on the TM fact sheet from the National Institute of Neurological Disorders and Stroke ("NINDS"),[60] which notes that TM "may be an autoimmune disease and may be triggered by vaccines." Pet'r's Ex. 22 at 6 (citing Pet'r's Ex. 36 at 1, ECF No. 25-5). The fact sheet notes that "[r]esearchers are uncertain of the exact causes of [TM]. The inflammation that causes such extensive damage to nerve fibers of the spinal cord may result from viral infections or abnormal immune reactions." *See id.* It continues that "[i]nfectious agents suspected of causing [TM] include

[58] K. Kaneko et al., *CSF Cytokine Profile in MOG-IgC+ Neurological Disease is Similar to AQP4-IgC+ NMOSD but Distinct from MS: a cross-sectional study and potential therapeutic implications,* 0:0 J. NEUROL. NEUROSURG. PSYSCHIATRY 1–10 (2018).

[59] *See Prevnar-13 Package Insert, supra* note 51.

[60] *Transverse Myelitis Fact Sheet,* NAT'L INST. OF NEURO. DISORDERS & STROKE (http://www.ninds.nih.gov/Disorders/Patient-Caregiver-Education/Fact-Sheets/Transverse-Myelitis-Fact-Sheet).

varicella zoster[61] . . . herpes simplex,[62] cytomegalovirus,[63] Epstein-Barr,[64] influenza, echovirus,[65] [HIV], hepatitis A,[66] [] rubella[,[67] b]acterial skin infections, middle ear infections (*otitis media*), and [bacterial pneumonia.]" Pet'r's Ex. 36 at 1. It also notes that "[TM] may also occur as a complication of . . . vaccinations, including those for chickenpox and rabies." *Id.* Dr. Steinman noted additional support for TM being an autoimmune condition. Pet'r's Ex. 22 at 7. He wrote that some individuals with TM also have other autoimmune diseases such as "systemic lupus erythematosus,[68] Sjögren's syndrome,[69] and sarcoidosis[.]"[70] *Id.*

Dr. Steinman noted evidence supporting his conclusion that R.S. experienced an autoimmune reaction to the Prevnar 13 vaccine resulting in TM. Pet'r's Ex. 60 at 1. He testified that R.S.'s TM was "[m]ost certainly" an inflammatory TM. Tr. 51:12–14. He relied on R.S.'s abnormal spinal fluid results ("slightly elevated" at 48) from April 2, 2013. Pet'r's Ex. 60 at 1 (citing Pet'r's Ex. 10 at 47; Pet'r's Ex. 9 at 3); *see also* Tr. 98:7–10. Dr. Steinman cited a study by

[61] Varicella zoster is "a virus of the genus 'varicellovirus' that is the etiologic agent of chickenpox and herpes zoster." *Dorland's* at 2065.

[62] Herpes simplex virus is "a group of acute infections caused by human herpesviruses 1 and 2, characterized by small fluid-filled vesicles on the skin or a mucous membrane with a raised erythematous base; it may be a primary infection or recurrent because of reactivation of a latent infection . . . Precipitating factors include fever, exposure to cold temperature or ultraviolet rays, sunburn, cutaneous or mucosal abrasions, emotional stress, and nerve injury." *Dorland's* at 2062.

[63] Cytomegalovirus "infect[s] humans and nonhuman primates, with the production of unique large cells bearing intranuclear inclusions. It includes the species human herpesvirus 5[.]" *Dorland's* at 466.

[64] Epstein-Barr is also referred to as human herpesvirus 4. *Dorland's* at 2061. Human herpesvirus 4 is "a virus of the genus lymphocryptovirus that causes infectious mononucleosis[.]" *Id.* at 852–53.

[65] Echovirus is "any of numerous species and strains of the family Picornaviridae, some of which cause aseptic meningitis or a febrile rash[.]" *Dorland's* at 590.

[66] Hepatitis A is "a usually self-limited viral disease of worldwide distribution caused by the hepatitis A virus, more prevalent in areas of poor hygiene and low socioeconomic standards. It is transmitted almost exclusively by the fecal-oral route, although parenteral transmission is possible; there is no carrier state. The incubation period is about 30 days, with a range of 15 to 50 days. Most cases are clinically inapparent or have mild flulike symptoms; jaundice, if present, is usually mild." *Dorland's* at 844.

[67] Rubella is "an acute, usually benign, infectious disease caused by viruses of genus Rubivirus, . . . affecting most often children and nonimmune young adults. The virus enters the respiratory tract via droplet nuclei and spreads to the lymphatic system. The first symptoms are a slight cold, sore throat, and fever, followed by enlargement of the postauricular, suboccipital, and cervical lymph nodes, and later appearance of a fine pink rash that begins on the head and spreads to become generalized." *Dorland's* at 1657.

[68] Lupus erythematosus is the "name formerly given to numerous types of localized destruction or degeneration of the skin caused by cutaneous diseases[.]" *Dorland's* at 1079.

[69] Sjögren's syndrome is "a symptom complex of unknown etiology, usually occurring in middle-aged or older women, marked by the triad of keratoconjunctivitis sicca with or without lacrimal gland enlargement, xerostomia with or without salivary gland enlargement, and the presence of a connective tissue disease, usually rheumatoid arthritis but sometimes systemic lupus erythematosus, scleroderma, or polymyositis. An abnormal immune response has been implicated." *Dorland's* at 1848.

[70] Sarcoidosis is "a chronic, progressive, systemic granulomatous reticulosis of unknown etiology, characterized by hard tubercles . . . It can affect almost any organ or tissue, including the skin, lungs, lymph nodes, liver, spleen, eyes, and small bones of the hands and feet." *Dorland's* at 1668. Reticulosis is "an abnormal increase in cells[.]" *Id.* at 1632.

Al Deeb et al.,[71] which provided a study on TM, including a "review of CSF [levels] in [thirty-two] patients, [two] were normal, and the remainder were abnormal." Pet'r's Ex. 60 at 1 (citing Pet'r's Ex. 62 at 1, ECF No. 45-4). The authors found that "[c]ells were raised in [twenty-six patients] . . . they were predominantly lymphocytes in all patients, and protein was high in [twenty-eight patients.]" Pet'r's Ex. 62 at 3. Dr. Steinman compared this study to R.S. and noted that her "protein was high and [her] cells were normal[.]" Pet'r's Ex. 60 at 2; *see also* Tr. 49:1–7. He opined that "these findings indicate an abnormal CSF and what is seen when there is neuroinflammation." Pet'r's Ex. 60 at 2.

He also relied on R.S.'s April 2, 2013 MRI findings which "definitively showed [TM.]" *Id.* (citing Pet'r's Ex. 10 at 47). Dr. Steinman wrote that "[b]y history, CSF findings and imaging[,] there is evidence of an inflammatory response in the central nervous system known as [TM]." Pet'r's Ex. 60 at 2. As further support, he also noted that R.S. received three treatments that are "aimed at treating inflammatory disease[s] of the spinal cord[,]" including IV steroids, IVIG, and plasmapheresis. Tr. 49:7–21. Dr. Steinman also noted that "infectious etiologies were ruled out by testing," including R.S.'s CSF and comprehensive metabolic panel. Pet'r's Ex. 60 at 2 (citing Pet'r's Ex. 9 at 7, 9, 13–14). Dr. Steinman therefore concluded that R.S.'s diagnosis is an inflammatory autoimmune TM. Pet'r's Ex. 60 at 2.

Dr. Steinman also wrote that "[t]he extensive [TM] from C2 to T4 [in R.S.] was likely the result of the strong recall response to the third dose of Prevnar 13 on March 18, 2013." Pet'r's Ex. 22 at 9. He noted the dates of R.S.'s earlier doses of Prevnar 13 and explained that antibodies to such phosphoglycerols in the vaccine could indeed interact with myelin components in the spinal cord, triggering TM. Tr. 52:23–25, 53:1–3; *see also* Pet'r's Ex. 6 at 1. He testified that the cause of R.S.'s TM was "a component in the Prevnar 13 vaccine that is critical for its immunogenicity . . . and the immune system attack[ed] one of the components of the vaccine." Tr. 52:23–25, 53:1–3. Dr. Steinman explained that he based this opinion on "three different levels of research." Tr. 53:4–5. He relied on investigations in his lab that have been published in peer-reviewed journals, the composition of the Prevnar 13 vaccine as described on the package insert, and a comparison between the immune response in MS and TM. Tr. 53:4–20.

From there, Dr. Steinman indicated that R.S. received the Prevnar 13 vaccine on March 18, 2013, and experienced the onset of TM "within two weeks[.]" Pet'r's Ex. 22 at 9. Specifically, he testified that R.S. developed the first symptoms of TM "around April 1st[.]" Tr. 50:2–4. Dr. Steinman stated that "thirteen days between [R.S.'s] immunization . . . would be right in the bullseye of when neuroinflammatory conditions are likely to [] manifest." Tr. 99:9–13. He wrote that this timeframe is "entirely consistent with what is seen following immunization and the onset of central nervous inflammation in acute disseminated encephalomyelitis [("ADEM")[72]]." Pet'r's

[71] S.M. Al Deeb et al., *Acute Transverse Myelitis – A Localized Form of Postinfectious Encephalomyelitis,* 120 BRAIN 1115–997 (1997).

[72] Acute disseminated encephalomyelitis ("ADEM") is "an acute or subacute encephalomyelitis or myelitis characterized by perivascular lymphocyte and mononuclear cell infiltration and demyelination; it occurs most often after an acute viral infection, especially measles, but may occur without a recognizable antecedent. It is believed to be a manifestation of an autoimmune attack on the myelin of the central nervous system. Symptoms include fever, headache, and vomiting; sometimes tremor, seizures, and paralysis; and

Ex. 22 at 10 (citing Pet'r's Ex. 44, ECF No. 25-5).[73] Dr. Steinman relied on the article by Bennetto and Scolding, which noted that the timing of the first symptoms of ADEM post vaccination "varies slightly with the precipitant: [] 1–14 days after non-neural vaccines, . . . and 1–3 weeks (or more) after rabies inoculation." Pet'r's Ex. 44 at 3. Dr. Steinman also relied on the study by Schonberger et al.,[74] which describes the onset time for GBS following the 1976 H1NI flu vaccination. Pet'r's Ex. 22 at 10 (citing Pet'r's Ex. 45, ECF No. 25-5). The authors found that there was an increased risk for developing GBS up to six weeks and "even in weeks two and three" post vaccination. Pet'r's Ex. 22 at 11. They wrote that "[71%] of the vaccinated cases . . . became ill within the first four weeks after vaccination and 52[%] in the second and third weeks after vaccination." Pet'r's Ex. 45 at 6. They explained that "[b]y two-day intervals between vaccination and onset, the largest percentage of cases (10%) occurred on the 16th and 17th days after vaccination[.]" *Id.* at 6–7. Dr. Steinman admitted that neither cited example covers the Prevnar 13 vaccine or TM, specifically. Pet'r's Ex. 22 at 12. He wrote that he "think[s] these are weak surrogates for [TM] and Prevnar 13, but it is the best we can use at this point in this context." *Id.*

Dr. Steinman admitted that infections "sometimes trigger [TM.]" Tr. 99:24–25, 100:1. He described post-infectious cases of TM. Pet'r's Ex. 22 at 7. He wrote that in post-infectious cases, "immune system mechanisms, rather than active viral or bacterial infections, appear to play an important role in causing damage to spinal nerves." *Id.* He explained that "stimulation of the immune system in response to infection indicates that an autoimmune reaction may be responsible[]" for post-infectious TM. *Id.* He nonetheless awarded the Prevnar 13 vaccine "a higher probability" of triggering TM in R.S. compared to "an unknown, [R.S.'s] recurrent respiratory infection[.]" Pet'r's Ex. 46 at 5.

On cross-examination, Dr. Steinman admitted that he has never diagnosed a patient with TM attributed to the Prevnar 13 vaccine or published on the same. Tr. 118:13–17. Dr. Steinman acknowledged that his submitted medical literature does not discuss molecular mimicry with respect to the Prevnar 13 vaccine and TM. Tr. 123:24–25, 124:1–2. However, he stated that while such literature does not "directly" discuss this concept, "the nuanced answer is" that it "lead[s] you right up to the gate." Tr. 124:3–7 (citing Pet'r's Exs. 38, 52). He further conceded that his provided medical literature does not contain case reports regarding a patient developing TM after the Prevnar 13 vaccine. Tr. 122:21–25, 123:1–17. Dr. Steinman was also confronted with the Chang et al.[75] article, which Respondent argued did not indicate that without phosphoglycerol, the vaccine would lose immunogenicity. Tr. 127:8–13 (citing Pet'r's Ex. 52). To support his conclusion, Dr. Steinman read verbatim from the Chang et al. abstract, stating that '"the loss of these groups . . . [glycerol phosphate and the O-acetyl group] may potentially reduce the ability of the 18C polysaccharide . . . to induce the desired immune response."' Tr. 127:18–23 (citing Pet'r's Ex. 52 at 1). He read that the '"glycerol phosphate must be preserved for conserving adequate antigenicity of the 18C capsular polysaccharide."' Tr. 127:25, 128:1–2 (citing Pet'r's Ex. 52 at 1).

---

lethargy progressing to coma that can be fatal. Many survivors have residual neurologic deficits." *Dorland's* at 613.

[73] L. Bennetto & N. Scolding, *Inflammatory/Post-Infectious Encephalomyelitis,* 75 J. NEUROL. NEUROSURG. PSYCH. 22–28 (2004).

[74] L. Schonberger, et al., *Guillain-Barré Syndrome Following Vaccination in the National Influenza Immunization Program, United States, 1976–1977,* 110:2 AM. J. EPIDEMIOL. 105–24 (1979).

[75] *See* Chang, et. al., *supra* note 53.

On rebuttal, Dr. Steinman noted that the focus of his research for the last forty years has been on "how the immune system attacks the brain . . . and spinal cord in [TM.]" Tr. 187:7–14. Dr. Steinman stated that the major difference between the way he views this case as compared to Dr. McGeady, is that he "based Petitioners' theory on actual data." Tr. 189:6–7. He admitted, however, that "the data are imperfect." Tr. 189:7.

3. Respondent's Expert, Dr. McGeady

Dr. McGeady submitted five expert reports and testified at the entitlement hearing. *See* Resp't's Exs. A, K, T, JJ, MM; Tr. 129–185. In his first report, Dr. McGeady concluded with a reasonable degree of medical certainty that the Prevnar 13 [vaccine] received by [R.S.] on [March 18, 2013,] did not cause her to develop TM on [April 1, 2013]." Resp't's Ex. A at 9; Resp't's Ex. K at 5. He noted his issues with Dr. Steinman's theory of molecular mimicry. Resp't's Ex. A at 4. Dr. McGeady wrote that Dr. Steinman "has embraced the phenomenon of molecular mimicry as a cause of disease for many years." *Id.* He noted, however, that "[h]is enthusiasm is not shared by all investigators[.]" *Id.* He testified that Dr. Steinman's theory of molecular mimicry causing TM has not been "convincingly proven." Tr. 166:1–3. He continued that "it is inaccurate to imply, as Dr. Steinman seems to do, that molecular mimicry is a common and well-established mechanism of autoimmune disease, or that it has ever been demonstrated to be a cause of TM." Resp't's Ex. K at 2. Dr. McGeady cited three articles to support his opinion that "[i]n the absence of more compelling evidence, authorities in the field of autoimmunity are quite circumspect about accepting molecular mimicry as a pathophysiologic mechanism[.]" Resp't's Ex. A at 4 (citing Resp't's Exs. C, D, E, ECF Nos. 29-3–29-5).[76]

Dr. McGeady noted his concerns with Dr. Steinman's first proposed theory prior to the entitlement hearing in January of 2020. He wrote that Dr. Steinman's "assertion appears to say that the Prevnar 13 vaccine[] contains phospholipid antigens which elicit [an] antibody that is capable of cross reacting with phospholipids in the CNS[,] resulting in TM." Resp't's Ex. A at 6. He continued that the problem with Dr. Steinman's theory is that it "infers that the Prevnar 13 [vaccine] actually contains phospholipids or pneumococcal organisms capable of producing phospholipids." *Id.* Dr. McGeady cited Dr. Steinman's reliance on the Prevnar 13 package insert which describes the process of manufacturing the Prevnar 13 vaccine. *Id.* (citing Pet'r's Ex. 22 at 6; Pet'r's Ex. 35). He noted that the package insert indicates that "[t]he individual polysaccharides are purified through centrifugation precipitation, ultrafiltration[,] and column chromatography." Resp't's Ex. A at 6 (citing Pet'r's Ex. 35). Dr. McGeady wrote that while he does "not dispute the fact that some pneumococci synthesize phospholipids in their biologic cycle . . . [he] could not find any statement that the phospholipids are actually present in the Prevnar 13 vaccine." Resp't's Ex. A at 6. As support, he noted that as the "Prevnar 13 [vaccine] contains a suspension of saccharides of capsular antigens that have been extensively purified by biochemical techniques, and does not contain intact organisms, it would seem probable that there are no phospholipids in the vaccine." *Id.* Based on this, Dr. McGeady opined that "[t]heir absence would reject Dr. Steinman's hypothesis of molecular mimicry." *Id.*

[76] L. Albert, et al., *Molecular Mimicry and Autoimmunity,* 341 N. ENGL. J. MED. 2068–74 (1999); M.B.A. Oldstone, *Molecular Mimicry, Microbial Infection, and Autoimmune Disease: Evolution of the Concept,* 296 CTMI 1–17 (2005); N. R. Rose, *Learning from Myocarditis: Mimicry, Chaos and Black Holes,* 6 F1000 PRIME REP. 25–25 (2014).

Dr. McGeady criticized Dr. Steinman's reliance on the Chang et al.[77] article to support his conclusion. Resp't's Ex. K at 3 (citing Pet'r's Ex. 52). He noted that the Chang et al. article showed "that the phosphoglycerol group in the S. pneumoniae 18[C] organism is essential to maximal immunogenicity." *See id.* He explained that the "phosphoglycerol group found in the [S]. pneumonia 18[C] polysaccharide does not constitute a phospholipid." Resp't's Ex. K at 3. Instead, Dr. McGeady noted that "[a] phospholipid is a complex molecule which consists of a phosphoglycerol group (i.e.[,] a molecule of glycerol to which a molecule of phosphoric acid has become attached), and usually two chains of long chain fatty acids[.]" Resp't's Ex. T at 2. Dr. McGeady continued that the structures described in Dr. Steinman's report "demonstrate a phosphoglycerol group, but this is not the same as a phospholipid." Resp't's Ex. K at 4 (citing Pet'r's Exs. 46, 52). He continued that the "phosphoglycerol group in the pneumococcal 18[C] polysaccharide does not include the fatty acid and therefore does not constitute a phospholipid." Resp't's Ex. T at 2. He maintained that Dr. Steinman's theory "does not demonstrate the presence of phospholipids in the polysaccharide." *Id.* at 3. Dr. McGeady also criticized Dr. Steinman's reliance on the Chang et al. article because the "polysaccharides in that study [were] conjugated to tetanus toxoid[,] while Prevnar [13] is a diphtheria toxoid conjugate." Resp't's Ex. K at 4 (citing Pet'r's Ex. 52). He opined that the "differences in the resulting vaccines could lend different relevance to the putative immunogenicity of the phosphoglycerol group." Resp't's Ex. K at 4.

Then, Dr. McGeady responded to Dr. Steinman's direct testimony whereby he altered his theory to focus on "the phosphoglycerol moiety of the Prevnar 13 vaccine" being necessary for maximum vaccine antigenicity instead of phospholipids. Resp't's Ex. JJ at 1. He addressed Dr. Steinman's contention "that phosphoglycerol constitutes a shared epitope with structures in the human [CNS]." *Id.* Dr. McGeady noted that Dr. Steinman "d[id] not, and indeed cannot, specify which epitope he speculates is shared with the CNS." *Id.* Dr. McGeady opined that "an epitope shared between the CNS and the vaccine Prevnar 13 cannot be specified, because it would have to consist of a phosphoglycerol group in conjunction with a polysaccharide found within the CNS to match that in the vaccine." Resp't's Ex. MM at 2. He wrote that "[s]uch a structure is not known." *Id.*

Dr. McGeady maintained that the issue with Petitioners' theory is that "the phosphoglycerol or phosphocholine is connected to a lipid in the human CNS and a saccharide in the Prevnar vaccine[.]" Tr. 141:10–14. He opined that "those two [molecules] would be perceived differently by the immune system." Tr. 141:14–15. He also maintained that this is because the antibody is "very discriminating in what it recognizes[]" and "the production and function of the antibody" is not only dependent on recognizing the phospho head, but also what it is attached to. Tr. 161:24–25, 162:1–5. Dr. McGeady noted that in Dr. Steinman's hypothesis, "the large carrier molecule in Prevnar 13 would presumably be the polysaccharide capsule of one or two pneumococcal serotypes with the phosphoglycerol component[.]" Resp't's Ex. JJ at 2. Dr. McGeady compared this to the antibody generated in patients with MS, as mentioned by Dr. Steinman, which recognizes phosphocholine attached to "some component of the human CNS[.]" *Id.* He wrote that the antibody in patients with MS "would certainly be different from [the] pneumococcal polysaccharide[]" found in the Prevnar 13 vaccine. *Id.* He noted that "when you look at phosphocholine or phosphoglycerol as it appears in the polysaccharide vaccine, it's one way, and an antibody made to that is . . . going to recognize that configuration." Tr. 141:24–25,

[77] *See* Chang, et. al., *supra* note 53.

142:1–3. Dr. McGeady continued that "[w]hen you look at that same configuration . . . in the [CNS], where it[is] attached to long-chain fatty acids, . . . the immune system is not going to see that in the same way." Tr. 142:4–10. Dr. McGeady testified that the phosphoglycerol or phosphocholine molecule in the polysaccharide vaccine is not in the same configuration as it is in the CNS. Tr. 143:16–21. Dr. McGeady opined that where the phospho polar head of the phosphoglycerol or phosphocholine combines to saccharides vs. lipids is "definitely different[.]" Tr. 140:1–3. He therefore indicated that the "antibody produced which recognizes phosphocholine[,] would be that generated by two dissimilar large molecules, having in common only phosphocholine attached as a [small molecule], or [] share phosphocholine as an epitope." Resp't's Ex. JJ at 2. Based on this, Dr. McGeady opined that "[i]t is unlikely that two such dissimilar molecules would generate [an] antibody with closely related binding capabilities given the exquisite selectivity of antibody binding." *Id.*

Dr. McGeady opined that "to suggest that the immune system produces antibod[ies] promiscuously to molecules such as phosphoglycerol regardless of their molecular position, is to ignore the complexity of antibody production[.]" Resp't's Ex. MM at 2. He explained that antibodies "combine with the molecular structure that caused them to be generated, in a 'lock and key' relationship." Resp't's Ex. JJ at 2. Therefore, the antibody "will bind to only the molecular structure that caused it to be produced or to very closely related structures." *Id.* Dr. McGeady concluded that given this specificity, "it is most unlikely that a phosphoglycerol group in Prevnar 13 caused production of an antibody that recognizes both phosphoglycerol in the conjugated polysaccharide vaccine and in the tissues of the spinal cord." Resp't's Ex. MM at 2. He wrote that this is because the "phosphocholine in [the] pneumococcal polysaccharide is antigenically different from [the] phosphocholine in tissues such as myelin protein of the human CNS." *Id.* Specifically, he wrote that the "unlikeliness of this phenomenon . . . is compounded by the fact that for it to occur[,] the phosphocholine . . . would have to be in nearly identical configuration in both Prevnar 13 and the unidentified carrier of MS patients in order to give rise to these similar antibodies." Resp't's Ex. JJ at 2; *see also* Resp't's Ex. KK at 3, ECF No. 93-2.[78] Dr. McGeady testified that the configuration must be "very, very similar" between the CNS and the Prevnar 13 vaccine "in order for [] cross-reaction to occur[]" and he "just do[es not] think we have that here." Tr. 142:11–24. Dr. McGeady stated that the polar head group of phosphoglycerol or the phosphocholine between the CNS and the Prevnar vaccine is not "enough to create the type of cross-reaction" that Dr. Steinman proposed. Tr. 143:1–5.

He continued that the "immune system[,] . . . requires antigens to be of a certain size before an immune response is generated . . . [and s]mall molecules with a weight of less than 10,000 daltons are not able to elicit an immune response as stand-alone immunogens." Resp't's Ex. JJ at 2 (citing Resp't's Ex. KK at 2); *see also* Tr. 140:15–17. Dr. McGeady noted that size becomes important based on whether it is "immunogenic by itself or whether it requires the presence of a larger molecule." Tr. 140:23–25. Dr. McGeady wrote that the molecular weight of phosphoglycerol is 200 daltons, "indicating that it is not immunogenic by itself." Resp't's Ex. JJ at 2; Tr. 137:8–9. He explained, however, that "antibodies can be produced to small molecules [haptens] if they are attached to large molecules [carriers]." Resp't's Ex. JJ at 2.

[78] T.G. PARSLOW, *Immunogens, Antigens, & Vaccines in* MEDICAL IMMUNOLOGY 73 (D.P. Stites et al. eds., 10th ed. 2001).

Dr. McGeady attacked Dr. Steinman's reliance on the Ho et al.[79] article. Tr. 146:5–25. He opined that this article did not support Petitioners' theory because the authors '"used mini array[s] comprising 17 lipids to profile autoantibody responses and cerebrospinal fluid from remitting/relapsing MS . . . ."' Tr. 146:15–18 (citing Pet'r's Ex. 38). He continued that '"[t]he analysis revealed antibody reactivity to three of the seven[]"' lipids. Tr. 146:19–20. Dr. McGeady testified that to him, "that kind of supports what [his] contention is, [] that this antibody is extremely discriminating[and i]f it just reacted with the phosphate polar head, it would have reacted with all seven of those." Tr. 146:21–25. Dr. McGeady emphasized that the Ho et al. authors looked at phosphate polar heads connected to lipids, only. Tr. 147:8–13. He noted that the authors did not "explore whether or not there would be a reaction when that polar head was configured on a different carrier, such as a saccharide, as opposed to [the] same with lipid[s.]" Tr. 185:6–14. When asked, Dr. McGeady repeated his distinction between MS and TM to opine that the Ho et al. article is not applicable to R.S.'s case. Tr. 180:15–23. He stated that he was not making a distinction between MS and TM for the purposes of molecular mimicry. Tr. 180:24–25. He simply maintained that they are separate diseases "[a]nd the pathology of them is distinct." Tr. 181:6–11.

Dr. McGeady further questioned Dr. Steinman's reliance on the Chang et al.[80] article, "showing that the phosphocholine is necessary for the immunogenicity of specific pneumococcal serotypes in a polysaccharide vaccine[.]" Resp't's Ex. JJ at 3. Dr. McGeady highlighted that this is "dissimilar to [the] Prevnar [13 vaccine,] in that it is conjugated to tetanus rather than diphtheria toxoid." *Id.* (citing Pet'r's Ex. 52). He noted that "[w]hat is not known from that research" is whether antibodies directed to phosphocholine are "actually produced by this vaccine . . . ." Resp't's Ex. JJ at 3. Based on this, Dr. McGeady opined that "[i]t is possible, perhaps likely, that the need for phosphocholine in [the polysaccharide vaccine] is in the role of a structural or bridging component, rendering the polysaccharide maximally immunogenic rather than providing any direct antigenic function by itself." *Id.* Dr. McGeady testified that the Chang et al. article showed that "when you immunized animals . . . they made antibod[ies] when you gave them the saccharide, but they made [the] antibody 1,000 times more when you gave them the saccharide attached to tetanus toxoid." Tr. 158:7–15. Dr. McGeady noted that "the vaccine [the Chang et al. authors] were looking at [] is actually different from the Prevnar in the sense that the Prevnar is attached to diphtheria toxoid; this was tetanus toxoid." Tr. 158:15–19. He stated that the Chang et al. article "showed that it needed the carrier protein in order to have maximal antigenicity." Tr. 158:24–25. Dr. McGeady acknowledged that it also showed that "the phosphocholine is necessary for [] antigenicity." Tr. 159:10–12.

He wrote that an additional flaw in Dr. Steinman's theory is that "the assertion that cross-immunity to myelin sheath components of the CNS elicits antibodies that result in TM is not consistent with the reported immunopathology of TM." Resp't's Ex. A at 7. Dr. McGeady alternatively proposed that "the known immunopathology of TM is considerably more suggestive of cell[-]mediated immune damage than it is of [an] antibody[-]mediated injury." Resp't's Ex. K at 4. He explained the difference between cell-mediated immune damage and antibody-mediated damage. Tr. 149:23–25. Cell-mediated immunity is "carried out by . . . T cells." Tr. 150:1–3. One such type of T cell is the "cytotoxic T cell that does what the name would suggest, it kills cells that are seen as something that should[not] be there[]" and "attracts other inflammatory cells, such as

[79] *See* Ho, et. al., *supra* note 43.
[80] *See* Chang, et. al., *supra* note 53.

monocytes and macrophages, to the site." Tr. 150:4–9. Dr. McGeady explained that antibodies "come[] as a result of these T cells activating the other cells called B cells that [] produce the antibody." Tr. 150:11–13. He continued that once the antibody is produced, "it recognizes this 'nonself' and binds to it[.]" Tr. 150:13–15. Once that happens, the antibody "interfer[es] with the cell." Tr. 151:6–7. He relied on an article by Awad et al.,[81] to explain that "biopsies taken during the acute phase of TM[] found infiltration of CD4+ and CD8+ T cells together with [the] perivascular spread of monocytes and evidence of astroglial and microglial activation." Resp't's Ex. A at 7 (citing Resp't's Ex. F, ECF No. 29-6). Dr. McGeady wrote that "this pathological description does not rule out a role for autoantibod[ies] in acute TM[.]" Resp't's Ex. A at 7. He maintained that "it suggests that other immune mechanisms are primarily operative[] in producing tissue injury." *Id.* The authors of the Awad et al. article noted, however, that such "infiltrates of CD4+ and CD8+ T-lymphocytes were found to be prominent[,] suggesting [an] immune-mediated disease process." Resp't's Ex. F at 3.

As support for this conclusion that cellular processes predominate the pathology of TM, Dr. McGeady described three mechanisms by which "[a]ntibody mediated tissue injury ordinarily occurs[.]" Resp't's Ex. T at 5. He noted that one mechanism is opsonization, "a process by which [an] antibody coats a target cell or tissue, [a] complement is activated[,] and phagocytic cells such as neutrophils and monocytes/macrophages ingest or attempt to ingest the target cell or tissue[.]" *Id.* (citing Resp't's Ex. GG at 1, ECF No. 76-13).[82] A second mechanism is by "causing inflammation such as when [an] antibody binds to a cell or tissue complement[,] is activated[,] and chemotactic molecules are generated causing the same phagocytic cells to accumulate and release potent tissue degrading enzymes." Resp't's Ex. T at 5 (citing Resp't's Ex. GG at 1). Dr. McGeady noted that such events "lead to [an] injury to the antibody coated cells or tissue[s] and to nearby structures[.]" Resp't's Ex. T at 5. This leads to the third mechanism, "interference with normal cellular function whereby [an] antibody binds to a critical structure of a cell causing [a] gain or loss of function, but not creating an inflammatory cell infiltrate." *Id.* (citing Resp't's Ex. GG at 1). Dr. McGeady wrote that in each of the mechanisms for an antibody mediated injury, the "cells signifying this type of immunopathology in its acute phase are neutrophils, but these are not reported to be present in biopsies . . . of TM[.]" Resp't's Ex. T at 5–6 (citing Resp't's Ex. F at 3).[83] Instead, he maintained that "CD4+ and CD8+ T cells and monocytes which are characteristic of cellular immune pathology[,]" are found instead. Resp't's Ex. T at 6 (citing Resp't's Ex. F at 3).

He indicated that further evidence in support of the immunopathology "not being antibody mediated is the recent description of the elevated levels of the pro-inflammatory cytokine IL-6 in the cerebrospinal fluid" of both adult and pediatric cases of TM. Resp't's Ex. K at 4 (citing Resp't's Exs. F, GG). Dr. McGeady defined IL-6 as "a proinflammatory chemical that[is] generated in the course of an inflammatory reaction." Tr. 151:8–10. He testified that a finding of elevated IL-6 is relevant in a case of pediatric TM because it is "known to be generated by T cells and by macrophages[]" but not by B cells, "the antibody producers." Tr. 151:14–19. "So[,] finding [IL-6] would make you think that [] one arm of the immune system is activated and the other is

[81] A. Awad, et al., *Idiopathic Transverse Myelitis and Neuromyelitis Optics: Clinical Profiles and Therapeutic Choices,* 9 CURRENT NEUROPHARMACOLOGY 417–28 (2011).
[82] A. ABBAS ET AL., *Cytokines in* CELLULAR & MOLECULAR IMMUNOLOGY 519 (Elsevier eds., 9th ed. 2018).
[83] *See* Awad, et. al., *supra* note 81.

quiescent." Tr. 151:19–21. Dr. McGeady explained that "IL-6 is produced by cells of the innate immune system, such as microglial cells, by endothelial cells[,] and by T cells. IL-6 is not known to be produced by B cells or generated in large quantities during antibody related reactions." Resp't's Ex. K at 4. He continued that "the finding of elevated IL-6 in TM is indicative of a cellular immune process or innate immune activation rather than an autoantibody driven process [] as Dr. Steinman hypothesizes." *Id.* at 4–5. Dr. McGeady therefore opined that "[t]he known immunopathology of TM is not consistent with Dr. Steinman's hypothesis of an autoantibody mediated injury to the spinal cord." *Id.* at 5.

Dr. McGeady further questioned Dr. Steinman's comparison of the antibody found in patients with MS and the antibody elicited by Prevnar 13, which can cause TM. Resp't's Ex. JJ at 3. Dr. McGeady noted that a study by Reich et al.,[84] "has questioned" the conclusion that antibody production is a cause of MS pathologic lesions. *Id.* (citing Resp't's Ex. LL, ECF No. 93-3). The authors noted that "[t]here is evidence that the antibody-producing function of B-lineage cells is important in some [MS] lesions." Resp't's Ex. LL at 6. They continued that "because of the rapidity of [the] response to B cell depletion (as early as 8–12 weeks), even before the reduction of circulating immunoglobulin, it seems more likely that other functions of B cells, including antigen presentation to helper T cells and cytokine production[,] are more relevant." Resp't's Ex. JJ at 3 (citing Resp't's Ex. LL at 6). Based on this observation, Dr. McGeady opined that the antibody directed at elements of the CNS in MS, "may be an epiphenomenon, resulting from the release of sequestered antigens by other immune mechanisms[,]" such as cell-mediated responses. Resp't's Ex. JJ at 3. He elaborated on this point and stated that the presence of antibodies found in a patient with TM "would favor a diagnosis that the antibody caused the thing[.]" Tr. 152:7–12. However, "sometimes cellular mechanisms damage or destroy a cell, which liberates antigens that are sequestered normally[]" which "[t]he immune system does[not] normally see[.]" Tr. 152:15–16. But now, "the immune system may make antibod[ies] to those released antigens." Tr. 152:16–17. Dr. McGeady stated that this is what he described as "an epiphenomenon," meaning this reaction is "not really the cause of the damage to begin with, although it may contribute secondarily to it." Tr. 152:17–20. He compared this notion to the sequela of an injury. Tr. 152:21–24. Dr. McGeady concluded that since cellular mechanisms are "primarily responsible for TM, and an antibody reacting with components of the CNS is possibly an epiphenomenon, the presence of such [an] antibody, even if it had been demonstrated in [R.S.], would have little weight in discerning a relationship between Prevnar 13" and R.S.'s TM. Resp't's Ex. JJ at 3.

Dr. McGeady opined that "Dr. Steinman's hypothesis about the pathophysiology of the TM in [R.S.] may be flawed." Resp't's Ex. A at 5. Dr. McGeady wrote that Dr. Steinman's theory is "highly speculative" and "make[s] it difficult to accept the Prevnar 13 vaccination as the causal explanation of R.S.'s TM[.]" Resp't's Ex. JJ at 2. He also noted that there is no evidence that R.S. experienced an autoimmune reaction aside from the temporal proximity to her vaccination. Resp't's Ex. T at 2. Dr. McGeady nonetheless agreed that R.S.'s elevated CSF indicated that she had an inflammatory TM. Tr. 153:25, 154:1–2. Dr. McGeady testified that the fact that R.S.'s TM may be inflammatory does not indicate "the type of immune response [being] . . . antibody-mediated" or not. Tr. 183:9–16.

[84] D.S. Reich, et al., *Multiple Sclerosis,* 378:2 N. ENGL. J. MED. 169–80 (2018).

He noted that "the only evidence that the Prevnar 13 vaccine [R.S.] received on [March 18, 2013,] was related to the TM appearing on [April 1, 2013,] . . . [was] the temporal association between the immunization and the onset of TM." Resp't's Ex. A at 9. More specifically, he "do[es] not believe that [R.S.'s condition] was precipitated by her receipt of the Prevnar 13 vaccine, which antedated the onset of her symptoms by [twelve] days or so." Tr. 136:1–9. He opined that "[i]n view of the number of immunizations currently recommended for children, it is inevitable that some unfortunate illnesses will occur in some proximity to an immunization without being caused . . . by the immunization." Resp't's Ex. A at 9. Dr. McGeady cited the VAERS database to highlight that "only [nine] cases of TM reported have been possibly associated with [the] Prevnar 13 [vaccine]." Resp't's Ex. K at 3. He opined that "[t]his small number of TM cases in recipients of a universally recommended vaccine over an extensive period of time . . . indicates that TM associated with an intercurrent illness is much more common than association with receipt of Prevnar 13." *Id.* Based on this, he concluded that "[t]his infrequency of association indicates that Prevnar 13 is unlikely to be the cause of [R.S.]'s TM." *Id.*

Dr. McGeady stated that the onset of R.S.'s TM would "fall within the appropriate time frame for an . . . immunologically mediated reaction" to occur. Tr. 160:5–12. Dr. McGeady wrote that while Dr. Steinman's theory regarding onset is consistent with Petitioners' submitted medical literature, "it is of uncertain significance in this case." Resp't's Ex. A at 9. Dr. McGeady testified that he would expect to see onset within a similar time frame even if R.S.'s TM was caused by a preceding illness or infection. Tr. 160:19–24.

Dr. McGeady then addressed R.S.'s history of infections. Resp't's Ex. A at 8. He opined that "it is far more common for a child to have experienced a non-specific illness before the onset of TM than it is to . . . hold Prevnar 13 accountable for [R.S.'s] TM when an infectious history is far more common . . . ." *Id.* Dr. McGeady relied on several articles that noted "the occurrence of a prior illness in between 30 to 100% of cases of idiopathic TM[.]" Resp't's Ex. K at 2 (citing Resp't's Exs. M–P, ECF Nos. 32-3–32-6).[85] Dr. McGeady testified that many cases of TM are idiopathic. Tr. 155:6–8. He also addressed evidence that R.S. had preceding illnesses prior to developing TM. Tr. 154:7–10. He noted that the medical literature indicates that "47[% of TM cases] are preceded by some sort of recurring illness – a cold or whatever." Tr. 154:9–10. Dr. McGeady emphasized that the literature did not list one particular illness but "many different ones." Tr. 154:10–11. He explained that he was not saying with "100[%] certain[ty] that [R.S.'s] recurrent infections [] caused her [TM.]" Tr. 154:19–23. Dr. McGeady admitted that he did not know what the infection was that could have preceded R.S.'s TM. Tr. 164:22–24, 165:1–3. Dr. McGeady stated that R.S.'s TM "probably was triggered by something[.]" Tr. 163:23–25. But he could not determine "whether it was triggered by an immune response that would target the spinal cord or not[.]" Tr. 164:4–8. Dr. McGeady further acknowledged that the damage to R.S.'s spinal cord "probably was" an immune response, but he could not opine as to what triggered the immune response that damaged her spinal cord. Tr. 164:9–16.

[85] A. Kaplin, et al., *Diagnosis and Management of Acute Myelopathies,* 11 THE NEUROLOGIST 2–20 (2005); M. Absoud, et al., *Pediatric Transverse Myelitis,* 87 NEUROLOGY 46–52 (2016); D.A. Kerr & H. Ayetey, *Immunopathogenesis of Acute Transverse Myelitis,* 15 CURT. OPIN. NEUROL. 339–47 (2002); A. Awad, et al., *Idiopathic Transverse Myelitis and Neuromyelitis Optics: Clinical Profiles and Therapeutic Choices,* 9 CURRENT NEUROPHARMACOLOGY 417–28 (2011).

On cross-examination, Dr. McGeady conceded that he is not "specifically aware of the immune processes at work in . . . immunological injur[ies] of the [CNS.]" Tr. 173:10–14. He also conceded that he is not experienced with "the immunological process of the development of CNS conditions[.]" Tr. 183:17–20. Dr. McGeady was confronted with the Awad et al.[86] article, which noted that '"about 30[%] of pediatric cases [of TM] are precede[d] with immunizations within one month of disease onset."' Tr. 170:19–23 (citing Resp't's Ex. F at 3). He did not disagree with that statement. Tr. 171:1. Dr. McGeady was also confronted with the Wolf et al.[87] article, which noted that '"[p]ediatric acute [TM] is typically [preceded] by a mild illness in the three weeks prior to symptoms onset[,] as reported in 50 to 100[%] of cases."' Tr. 171:17–20 (citing Resp't's Ex. I at 2, ECF No. 29-9). The authors also noted that '"[o]ther less common provoking factors reported include vaccine, allergy shot, and mild trauma."' Tr. 171:20–21 (citing Resp't's Ex. I at 2). Dr. McGeady agreed with those statements. Tr. 171:22–24. Dr. McGeady qualified those statements and testified that "specific infections . . . have not been identified as associated with [TM]." Tr. 172:1–9. He stated that the same is also true regarding vaccines, a specific one has not been connected to TM. Tr. 172:12–16. Dr. McGeady was also confronted with the Kerr et al.[88] article, which noted that "it is widely reported in neurology texts that [acute TM] is a post-vaccination event." Tr. 173:1–5 (citing Resp't's Ex. BB at 2, ECF No. 76-8). He stated that he did not "know enough about what is in neurology texts to respond to that." Tr. 173:8–9.

Under my questioning, Dr. McGeady admitted that Dr. Steinman's theory is not "impossible[,]" because "almost nothing is impossible[.]" Tr. 176:7. Instead, he opined that "the improbability of [it] actually occurring is so vanishingly small that . . . [he] just do[esn't] think it happened[]" to R.S. Tr. 176:7–13.

IV. Applicable Legal Standards

To receive compensation under the Vaccine Act, a petitioner must demonstrate either that: (1) the petitioner suffered a "Table injury" by receiving a covered vaccine and subsequently developing a listed injury within the time frame prescribed by the Vaccine Injury Table set forth at 42 U.S.C. § 300aa-14, as amended by 42 C.F.R. § 100.3; or (2) that petitioner suffered an "off-Table injury," one not listed on the Table, as a result of his receiving a covered vaccine. *See* 42 U.S.C. §§ 300aa-11(c)(1)(C); *Moberly v. Sec'y of Health & Hum. Servs.*, 592 F.3d 1315, 1321 (Fed. Cir. 2010); *Capizzano v. Sec'y of Health & Hum. Servs.*, 440 F.3d 1317, 1319–20 (Fed. Cir. 2006). Petitioners do not allege a Table injury in this case; thus, they must prove that R.S.'s injury was caused-in-fact by a Table vaccine.

To establish causation-in-fact, a petitioner must demonstrate by a preponderance of the evidence that the vaccine was the cause of the injury. 42 U.S.C. § 300aa-13(a)(1)(A). A petitioner is required to prove that the vaccine was "not only a but-for cause of the injury but also a substantial factor in bringing about the injury." *Moberly*, 592 F.3d at 1321–22 (quoting *Shyface v. Sec'y of Health & Hum. Servs.*, 165 F.3d 1344, 1352–53 (Fed. Cir. 1999)).

---

[86] *See* Awad, et. al., *supra* note 81.

[87] V. Wolf, et al., *Pediatric Acute Transverse Myelitis Overview and Differential Diagnosis,* 27(11) J. CHILD NEURO. 1426–36 (2012).

[88] D.A. Kerr & H. Ayetey, *Immunopathogenesis of Acute Transverse Myelitis,* 15 CURT. OPIN. NEUROL. 339–47 (2002).

In the seminal case of *Althen v. Sec'y of the Dept. of Health & Hum. Servs*, the Federal Circuit set forth a three-pronged test used to determine whether a petitioner has established a causal link between a vaccine and the claimed injury. *See* 418 F.3d 1274, 1278–79 (Fed. Cir. 2005). The *Althen* test requires petitioners to set forth: "(1) a medical theory causally connecting the vaccination and the injury; (2) a logical sequence of cause and effect showing that the vaccination was the reason for the injury; and (3) a showing of a proximate temporal relationship between vaccination and injury." *Id.* at 1278. To establish entitlement to compensation under the Program, a petitioner is required to establish each of the three prongs of *Althen* by a preponderance of the evidence. *Id.* "[C]lose calls regarding causation are resolved in favor of injured claimants." *Id.* at 1280. Further, evidence used to satisfy one prong of the test may overlap to satisfy another prong. *Capizzano,* 440 F.3d at 1326.

A petitioner who satisfies all three prongs of the *Althen* test has established a prima facie showing of causation. *Hammitt v. Sec'y of Health & Hum. Servs*., 98 Fed. Cl. 719, 726 (2011). A petitioner who demonstrates by a preponderance of the evidence that he suffered an injury caused by vaccination is entitled to compensation unless the respondent can demonstrate by a preponderance of the evidence that the injury was caused by factors unrelated to the vaccination. *See Althen*, 418 F.3d at 1278; *Knudsen v. Sec'y of Health & Hum. Servs.*, 35 F.3d 543, 547 (Fed. Cir. 1994). In such a case, the government must not merely prove the existence of an alternative cause, but that such an alternative actually caused the injury. *Knudsen,* 35 F.3d at 549. Consequently, when and if a petitioner establishes a prima facie case, the burden then shifts to the government to prove that an alternative cause, unrelated to the administration of the vaccine, was the "sole substantial factor" in causing the alleged injury. *de Bazan v. Sec'y of Health & Hum. Servs.*, 539 F.3d 1347, 1354 (Fed. Cir. 2008); *see also Hammitt*, 98 Fed. Cl. at 726 (explaining that the respondent's burden is to show that the "factor unrelated" was the "sole substantial factor" in causing the injury). Additionally, a factor unrelated "may not include 'any idiopathic, unexplained, unknown, hypothetical, or undocumentable cause, factor, injury, illness or condition.'" 42 U.S.C. § 300aa-13(a)(2); *see also Doe v. Sec'y of Health & Hum. Servs.*, 601 F.3d 1349 (Fed. Cir. 2010) (opining that an idiopathic diagnosis cannot be a "factor unrelated," as it is idiopathic).

In considering the reliability of a petitioner's evidence of a prima facie case, the special master may consider alternative causes for a petitioner's condition that are reasonably raised in the record, even if the respondent does not pursue a formal alternative cause argument. *Doe,* 601 F.3d at 1358. Thus, in weighing a petitioner's case-in-chief, a special master may consider evidence that the petitioner's alleged injury could have been caused by alternative causes. *Id.* Proof of a "logical sequence of cause and effect" will eliminate potential likely alternatives. *Walther v. Sec'y of Health & Hum. Servs.*, 485 F.3d 1146, 1151 (Fed. Cir. 2007).

V. Discussion

A. Experts

Although special masters have the discretion to be informed by past rulings and experiences, case-specific filings and testimony are the most helpful types of evidence, given the fact-specific nature of each decision. *See Doe v. Sec'y of Health & Hum. Servs.*, 76 Fed. Cl. 328, 338–39 (2007). To that end, experts are an essential piece of a petitioner's claim and Respondent's

defense. Where both sides offer expert testimony, a special master's decision may be "based on the credibility of the experts and the relative persuasiveness of their competing theories." *Broekelschen v. Sec'y of Health & Hum. Servs.*, 618 F.3d 1339, 1347 (Fed. Cir. 2010) (citing *Lampe v. Sec'y of Health & Hum. Servs.*, 219 F.3d 1357, 1361 (Fed. Cir. 2000)).

This case ultimately turns not only on R.S.'s medical history, but also the persuasiveness of the written reports, supporting documentation, and expert testimony. I therefore must assess each expert's expertise in relation to the facts of Petitioners' case and assign weight accordingly. This assessment will inform my analysis pursuant to each prong of *Althen*.

I base this ruling on entitlement, in part, on Dr. Steinman's credentials and expertise in neurology and demyelinating diseases specifically, as compared to Dr. McGeady's main focus in allergy and immunology. I also base my decision on Dr. Schreiner's specified knowledge and experience treating children with TM and other demyelinating conditions. Taken together, Petitioners' experts' particularized area of expertise on demyelinating conditions of the spinal cord significantly outweighs Respondent's expert's limited experience with the same. While I in no way discount Dr. McGeady's understanding and experience involving neurology and demyelinating conditions, I must afford Petitioners' experts' highly specialized knowledge in neurology and demyelinating diseases more weight. Notably, in relevant part, Dr. Steinman completed a fellowship in chemical neurobiology at Harvard Medical School in 1971. Pet'r's Ex. 23 at 1. Dr. Steinman has held academic appointments in neurology since 1980. *Id.* The focus of his research for the last approximately forty years has been on how the immune system attacks the brain and spinal cord. Tr. 187:7–14. He has published extensively on the topic. *See* Pet'r's Ex. 23 at 5–45. He testified that his current clinical practice involves "treat[ing] patients with [TM,]" including children and infants, like R.S. Tr. 48:15–19. Dr. Schreiner similarly completed a fellowship in neuroimmunology at the University of Colorado in 2012. Pet'r's Ex. 71 at 1. She has been working as a pediatric neuroimmunologist since that time. *Id.* She currently treats patients with immune-mediated demyelinating conditions, including TM in children. *Id.* Dr. Schreiner is among a small group of pediatric neuroimmunologists that specialize in demyelinating disorders, and she publishes and presents extensively on the topic. *Id.*

Dr. McGeady is an extremely qualified expert in his field. He has a history of providing useful testimony and persuasive explanations in cases before me, as well as other special masters in the Program. In this case however, his ultimate opinion was delivered with more concessions and uncertainties than Petitioners' main expert, Dr. Steinman. *See Broekelschen*, 618 F.3d at 1347 (citing *Lampe*, 219 F.3d at 1362) (finding that where both sides offer expert testimony, a special master's decision may be "based on the credibility of the experts and the relative persuasiveness of their competing theories."). Dr. McGeady admitted that he is not a neurologist and does not directly treat patients with demyelinating conditions, such as TM. Tr. 132:23–25, 133:1–17. He also accepted at times that Dr. Steinman might be in a better position to answer questions about the process that leads to neurologic injury in TM because he is not familiar with it. *See* Tr. 183:17–20, 184:3–5. Dr. Steinman's background and knowledge in neurology and demyelinating conditions is more applicable to this case than Dr. McGeady's expertise in allergy and immunology when considering the parties' arguments in relation to the biological mechanism and immunologic response involved in R.S.'s demyelinating condition. Therefore, I must give Dr. Steinman's testimony considerable weight throughout my analysis.

B. *Althen* Prong One

Under the first prong of *Althen*, a petitioner must offer a scientific or medical theory that answers in the affirmative the question: "can the vaccine[] at issue cause the type of injury alleged?" *See Pafford v. Sec'y of Health & Hum. Servs.*, No. 01-0165V, 2004 WL 1717359, at *4 (Fed. Cl. Spec. Mstr. July 16, 2004), *mot. for rev. denied*, 64 Fed. Cl. 19 (2005), *aff'd*, 451 F.3d 1352 (Fed. Cir. 2006). To satisfy this prong, a petitioner's theory must be based on a "sound and reliable medical or scientific explanation." *Knudsen*, 35 F.3d at 548. Such a theory must only be "legally probable, not medically or scientifically certain." *Id.* at 548–49. A petitioner is not required to identify "specific biological mechanisms" to establish causation, nor are they required to present "epidemiologic studies, rechallenge[] the presence of pathological markers or genetic disposition, or general acceptance in the scientific or medical communities." *Capizzano,* 440 F.3d at 1325 (quoting *Althen*, 418 F.3d at 1280). Scientific and "objective confirmation" of the medical theory with additional medical documentation is unnecessary. *Althen*, 418 F.3d at 1278–81; *see also Moberly*, 592 F.3d at 1322. However, as the Federal Circuit has made clear, "simply identifying a 'plausible' theory of causation is insufficient for a petitioner to meet her burden of proof." *LaLonde v. Sec'y of Health & Hum. Servs.*, 746 F.3d 1334, 1339 (Fed. Cir. 2014) (citing *Moberly*, 592 F.3d at 1322). Rather, "[a] petitioner must provide a reputable medical or scientific explanation that pertains specifically to the petitioner's case." *Moberly*, 592 F.3d at 1322. In general, "the statutory standard of preponderance of the evidence requires a petitioner to demonstrate that the vaccine more likely than not caused the condition alleged." *LaLonde,* 746 F.3d at 1339.

Furthermore, establishing a sound and reliable medical theory connecting the vaccine to the injury often requires a petitioner to present expert testimony in support of her claim. *Lampe*, 219 F.3d at 1361. The Supreme Court's opinion in *Daubert v. Merrell Dow Pharmaceuticals, Inc.*, 509 U.S. 579 (1993), requires that courts determine the reliability of an expert opinion before it may be considered as evidence. "In short, the requirement that an expert's testimony pertain to 'scientific knowledge' establishes a standard of evidentiary reliability." *Id*. at 590 (citation omitted). Thus, for Vaccine Act claims, a "special master is entitled to require some indicia of reliability to support the assertion of the expert witness." *Moberly*, 592 F.3d at 1324. The *Daubert* factors are used in the *weighing* of the reliability of scientific evidence proffered. *Davis v. Sec'y of Health & Hum. Servs.*, 94 Fed. Cl. 53, 66-67 (2010) ("uniquely in this Circuit, the *Daubert* factors have been employed also as an acceptable evidentiary-gauging tool with respect to persuasiveness of expert testimony already admitted"). Where both sides offer expert testimony, a special master's decision may be "based on the credibility of the experts and the relative persuasiveness of their competing theories." *Broekelschen*, 618 F.3d at 1347 (citing *Lampe*, 219 F.3d at 1362). And nothing requires the acceptance of an expert's conclusion "connected to existing data only by the *ipse dixit* of the expert," especially if "there is simply too great an analytical gap between the data and the opinion proffered." *Snyder v. Sec'y of Health & Hum. Servs.*, 88 Fed. Cl. 706, 743 (2009) (quoting *Gen. Elec. Co. v. Joiner*, 522 U.S. 136, 146 (1997)).

Petitioners have met their burden under *Althen* prong one. Petitioners posited a scientific or medical theory describing the Prevnar 13 vaccine's role in the development of TM via molecular mimicry. The parties in this case generally agree that TM can be an autoimmune disorder. While Respondent's expert maintains that the medical community is still "quite circumspect" about

accepting molecular mimicry as a valid mechanism, Respondent's own submitted medical literature indeed recognizes that "[m]olecular mimicry is one mechanism by which infectious agents (or other exogenous substances) may trigger an immune response against autoantigens." Resp't's Ex. C at 1, 5.[89] I noted during the hearing in January of 2021, that Dr. Steinman has provided a specific biological mechanism, and that I was seeking for Dr. McGeady to highlight flaws in that mechanism. Tr. 179:16–19. Instead, he acknowledged that Petitioners' theory is not impossible, because nothing is "impossible," he just does not believe it applies in R.S.'s case pursuant to *Althen* prong two. Tr. 176:7–13.

Additionally, while prior decisions of special masters are not binding on my analysis, it is persuasive that molecular mimicry has been accepted in the Program as a biological mechanism involving demyelinating conditions, including TM. *See, e.g.*, *Roberts v. Sec'y of Health & Hum. Servs.,* No. 09-427V, 2013 WL 5314698 (Fed. Cl. Spec. Mstr. Aug. 29, 2013); *Schmidt v. Sec'y of Health & Hum. Servs.,* No. 07-20V, 2009 WL 5196169 (Fed. Cl. Spec. Mstr. Dec. 17, 2009); *Hargrove v. Sec'y of Health & Hum. Servs.,* No. 05-0694V, 2009 WL 1220986 (Fed. Cl. Spec. Mstr. Apr. 14, 2009). It is also persuasive that special masters have determined that the Prevnar 13 vaccine can cause GBS, a similar demyelinating condition, via molecular mimicry. *See, e.g.*, *Pierson v. Sec'y of Health & Hum. Servs.*, No. 17-1136V, 2022 WL 322836 (Fed. Cl. Spec. Mstr. Jan. 19, 2022); *Koller v. Sec'y of Health & Hum. Servs.,* No. 16-439V, 2021 WL 5027947 (Fed. Cl. Spec. Mstr. Oct. 8, 2021). In many of these cases, petitioners relied on the comparison between similar demyelinating conditions, such as MS and GBS, to meet their burdens with respect to prong one.

Indeed, in his reports and testimony, Dr. Steinman relied heavily on articles that discuss MS. While Dr. McGeady argued that these articles are inapplicable because the pathological process involved in molecular mimicry would be different in patients with MS compared to those with TM, he did not explain why or how. In fact, Dr. McGeady's only support for his position is that they are separate diseases. Tr. 181. Dr. Steinman's expertise in MS is apparent during his explanation of why he is comparing one condition with the other. Dr. Steinman explained that they are both neuroinflammatory conditions of the CNS and "both can involve the spinal cord." Tr. 103:12–13. He stated that the distinguishing criteria involves the longevity of the disease (MS is a relapsing and remitting condition, while TM is monophasic). Tr. 103:15–23. Most importantly, Dr. Steinman noted that MS is often misdiagnosed as TM because "[y]ou really can[not]" diagnose MS prior to a relapse. Tr. 104:23–25. Dr. Steinman has credibly explained why the two conditions would be synonymous in pathogenesis.

Dr. Steinman's reliance on the Ho et al.[90] article is persuasive even though it discusses phospholipids instead of polysaccharides. The authors used an animal model and several mini arrays to identify the molecular target of the autoimmune response in patients with MS. *See* Pet'r's Ex. 38 at 1. They found that the immune response in MS patients targets the phospho polar head group in phosphoglycerol and phosphocholine of the phospholipids in the myelin sheath of the spinal cord. *Id.* at 4; *see also* Tr. 56:22–25, 57:1–10. Specifically, the authors relied on a mini array, which showed that the target of the immune response in patients with MS was the phosphate group of the phosphoglycerol molecule in the phospholipid in six of the seven lipids analyzed. *See*

[89] L. Albert, et al., *Molecular Mimicry and Autoimmunity,* 341 N. ENGL. J. MED. 2068–74 (1999).
[90] *See* Ho, et. al., *supra* note 43.

id. Dr. McGeady attempted to discredit these findings by noting that a sub-study only yielded points of attack in the phosphate group of phosphoglycerol in the phospholipid in three out of seven lipids analyzed. Nonetheless, he still agreed that the article showed that antibodies in MS patients attacked the phosphate polar head group of phosphoglycerol in the phospholipids of the myelin sheath. Tr. 167:7–10. Despite this concession, Dr. McGeady maintained that this article does not support Petitioners' claim because the authors did not determine whether the phosphoglycerol polar head group on lipids in the CNS would cross-react to the phosphoglycerol polar head group on polysaccharides found in the Prevnar 13 vaccine. He opined that the specific and "discriminatory" nature of antibody responses would prohibit the immune response from recognizing and attacking the phospho head group of phosphoglycerol if it is attached to two different molecules (phospholipids vs. polysaccharides). However, Dr. Steinman explained that it does not matter what the phosphoglycerol is attached to, the immune system "like a laser" hits the phospho head group of the phosphoglycerol. Tr. 191:1–6. Petitioners' reliance on the Ho et al. article advances their case with respect to *Althen* prong one because it shows that the immune response in a similar demyelinating condition to TM targets the phosphate group of the phosphoglycerol in the phospholipids of the myelin sheath.

Dr. Steinman described how phosphoglycerol is relevant to the Prevnar 13 vaccine. Dr. Steinman's reliance on the record to show that the phosphoglyercol molecule, which is attacked in patients with MS, is also present in the PCV 13 vaccine, is persuasive. Notably, Dr. Steinman's correction in nomenclature and revised theory accounts for both Dr. McGeady's original and amended criticisms of Petitioners' mechanism.

Indeed, Dr. Steinman successfully established that phosphoglycerol is contained in the PCV 13 vaccine. His position is overwhelmingly supported by the evidence that shows phosphoglycerol is a necessary component of the PCV 13 vaccine because the immune response to the phosphate group of this molecule produces antibodies. Such an attack on the polar head group of phosphoglycerol generates immunogenicity and makes the vaccine effective. The package insert and U.S. patent for the Prevnar 13 vaccine show that pneumococcal conjugate vaccines, such as the PCV 13 vaccine, must include the phosphoglycerol and phosphocholine molecules in the polysaccharide capsule of the streptococcus pneumoniae bacteria. *See* Pet'r's Exs. 35, 96. They also indicate that the PCV 13 vaccine contains streptococcus pneumoniae serotypes 18C and 19A for the purpose of creating an immune response to such bacteria. *See id.*

Dr. Steinman's position is also well-supported by the relevant medical literature. *See* Pet'r's Exs. 40, 52; *see also* Tr. 58:6–13, 61:10–14, 63:6–7. Dr. Steinman's reliance on the Chuang et al.[91] article is informative and corroborates the information contained in the PCV 13 package insert and patent. *See* Pet'r's Ex. 40 at 1. The authors noted that the phosphorylcholine polar group in serotype 19A of streptococcus pneumoniae is required for the success of infection and the ability to generate an immune response to serotype 19A. *Id.*; *see also* Tr. 93. This is because the immune response targets the phospho polar head group of that molecule. As demonstrated by the patent and package insert, serotype 19A is also in the PCV 13 vaccine. The authors of the Chang et al.[92] article documented the same importance of serotype 18C. The authors relied on a diagram of the capsular polysaccharide in s. pneumoniae serotype 18C. *See* Pet'r's Ex. 52 at 2; Tr. 88. They found

[91] *See* Chuang, et. al., *supra* note 54.
[92] *See* Chang, et. al., *supra* note 53.

that an effective vaccine against serotype 18C must produce an immune response against the phospho polar head group of phosphoglycerol in serotype 18C. *See id.* Serotype 18C is also contained in the PCV 13. It therefore stands to reason that a response to the phospho polar head group of phosphoglycerol in serotypes 18C and 19A is critical for generating an immune response to and the subsequent immunogenicity of PCV 13. This evidence therefore supports Petitioners' claim that phosphoglycerol is present in the vaccine.

Dr. Steinman then credibly explained that the immune system can target the phosphate group of the phosphoglycerol and phosphocholine molecules of the phospholipids in the myelin sheath and the phosphoglycerol and phosphocholine molecules in the polysaccharide capsule of the s. pneumonia in the PCV 13 vaccine because the phospho head group of the phosphoglycerol molecules are identical. This similarity allows a molecular mimic to occur. Dr. Steinman's reliance on the Lugowski et al.[93] article to show that the phosphosaccharide of the capsular polysaccharide in s. pneumoniae serotype 18C is in fact a phosphoglycerol molecule is helpful to Petitioners' case. *See* Pet'r's Ex. 53 at 2; Tr. 90:8–20. This establishes that the phosphoglycerol molecule attached to a polysaccharide indeed contains a phospho polar head group in essentially the same structure as the phospho head group of the phospholipids in the myelin sheath. Taken together with the Ho et al.[94] article, which shows a diagram of the phospho polar head group of the phosphorylcholine of the phospholipid, Dr. Steinman has established that the molecular structure of the phospho polar head group in the polysaccharide capsule of s. pneumoniae, such as serotype 18C contained in the PCV 13 vaccine, is "identical" to the phospho polar head group in the phosphoglycerol of the phospholipids of the myelin sheath. *See* Pet'r's Exs. 38, 53; Tr. 90–91. Respondent's expert's testimony that the immune system would not recognize the polar head group because it is attached to different molecules does not overcome Petitioners' theory. Indeed, as previously noted, Dr. Steinman credibly explained that it does not matter what the polar head group is attached to because the immune attack, "like a laser" is on that phospho polar head group of phosphoglycerol. Respondent's expert failed to provide evidence showing that this identification and cross-reaction of a single molecule would not be specific enough to induce an immune response. *See, e.g.*, Tr. 142:25, 143:1–15. Petitioners have therefore shown by a preponderant standard that the immune response to the phospho polar head group of phosphoglycerol triggered by the PCV 13 vaccine can erroneously target the same phosphoglycerol polar head group of phospholipids in the myelin sheath of the spinal cord via molecular mimicry, resulting in TM.

Dr. Steinman's theory implies that the immunopathology of TM is immune- or antibody-mediated. While Dr. McGeady disagrees, I find Dr. Steinman's opinion that an "[a]ntibody mediated injury is a cornerstone of our understanding of [TM]" but that the immunopathology is both antibody and cell-mediated, to be well-supported by the record. *See* Tr. 188:2–4; *see also* Pet'r's Ex. 60 at 6; Pet'r's Ex. 65 at 1. In fact, Dr. McGeady even testified consistent with Dr. Steinman's assertion. Dr. McGeady stated that cell-mediated immunity is "carried out by . . . T cells[]" and that antibodies "come[] as a result of these T cells activating the other cells called B cells that [] produce the antibody" to interfere with the cell. Tr. 150:1–13, 151:6–7. Dr. McGeady's testimony therefore supports Dr. Steinman's position because it accounts for both cellular and antibody involvement in the immunopathology of TM.

[93] *See* Lugowski & Jennings, *supra* note 52.
[94] *See* Ho, et. al., *supra* note 43.

While Petitioners did not provide literature specifically addressing whether the Prevnar 13 vaccine can cause TM via molecular mimicry, Petitioners are not required to provide such literature to prove their claim. *See Capizzano,* 440 F.3d at 1325 (quoting *Althen*, 418 F.3d at 1280) (finding that a petitioner is not required to identify "specific biological mechanisms" to establish causation, nor are they required to present "epidemiologic studies, rechallenge[] the presence of pathological markers or genetic disposition, or general acceptance in the scientific or medical communities."). After consideration of Dr. Steinman's expert opinion and comparative literature, I find Petitioners have satisfied prong one of *Althen*.

C. *Althen* Prong Two

Under the second prong of *Althen*, a petitioner must prove that the vaccine actually did cause the alleged injury in a particular case. *See Pafford*, 2004 WL 1717359, at *4; *Althen*, 418 F.3d at 1279. The second *Althen* prong requires proof of a logical sequence of cause and effect, usually supported by facts derived from a petitioner's medical records. *Althen*, 418 F.3d at 1278; *Capizzano*, 440 F.3d at 1326; *Grant v. Sec'y of Health & Hum. Servs.*, 956 F.2d 1144, 1148 (Fed. Cir. 1992). A petitioner does not meet this obligation by showing only a temporal association between the vaccination and the injury; instead, the petitioner "must explain *how* and *why* the injury occurred." *Pafford*, 2004 WL 1717359, at *4 (emphasis in original). The special master in *Pafford* noted petitioners "must prove [] both that her vaccinations were a substantial factor in causing the illness . . . and that the harm would not have occurred in the absence of the vaccination." 2004 WL 1717359, at *4 (citing *Shyface*, 165 F.3d at 1352). A reputable medical or scientific explanation must support this logical sequence of cause and effect. *Hodges v. Sec'y of Health & Hum. Servs.,* 9 F.3d 958, 961 (Fed Cir. 1993) (citation omitted). Nevertheless, "[r]equiring epidemiologic studies . . . or general acceptance in the scientific or medical communities . . . impermissibly raises a claimant's burden under the Vaccine Act and hinders the system created by Congress . . . ." *Capizzano*, 440 F.3d at 1325–26. "[C]lose calls regarding causation are resolved in favor of injured claimants." *Althen*, 418 F.3d at 1280.

In Program cases, contemporaneous medical records and the opinions of treating physicians are favored. *Capizzano*, 440 F.3d at 1326 (citing *Althen*, 418 F.3d at 1280). Indeed, when reviewing the record, a special master must consider the opinions of treating physicians. *Capizzano*, 440 F.3d at 1326. This is because "treating physicians are likely to be in the best position to determine whether 'a logical sequence of cause and effect show[s] that the vaccination was the reason for the injury.'" *Id.* In addition, "[m]edical records, in general, warrant consideration as trustworthy evidence. The records contain information supplied to or by health professionals to facilitate diagnosis and treatment of medical conditions. With proper treatment hanging in the balance, accuracy has an extra premium. These records are also generally contemporaneous to the medical events." *Cucuras v. Sec'y of Health & Hum. Servs.*, 993 F.2d 1525, 1528 (Fed. Cir. 1993). While a special master must consider these opinions and records, they are not "binding on the special master or court." 42 U.S.C. § 300aa-13(b)(1). Rather, when "evaluating the weight to be afforded to any such . . . [evidence], the special master . . . shall consider the entire record . . . ." *Id.* The record often includes "evidence of possible sources of injury" that can show alternate causes for the alleged vaccine-related injury. *See Stone v. Sec'y of Health & Hum. Servs.,* 676 F.3d 1373, 1379 (Fed. Cir. 2012).

The parties do not dispute that R.S. suffered an inflammatory, immune-mediated TM. *See* Tr. 51:12–14, 163:2–4. Petitioners' support for *Althen* prong two is based, in part, on Dr. Schreiner's opinion as R.S.'s treating neurologist and an expert in pediatric demyelinating conditions. Dr. Schreiner has been one of R.S.'s treaters since her initial presentation of TM in 2013. She opined that the cause of R.S.'s TM was "more likely than not the immunizations that [she] received on March 18, 2013[.]" Pet'r's Ex. 71 at 1. However, Dr. Schreiner did opine that R.S.'s TM was idiopathic through the course of R.S.'s treatment. *See* Pet'r's Ex. 5 at 172; Pet'r's Ex. 72 at 27. Dr. Schreiner documented her opinion that R.S.'s TM was idiopathic as recently as August of 2019, approximately six years into her care of R.S. Pet'r's Ex. 72 at 27. Despite Dr. Schreiner's equivocation, her expert opinion letter nonetheless provides support for Petitioners' claim because Dr. Schreiner was able to successfully substantiate the bases for her amended conclusion.

Dr. Schreiner's position warrants substantial consideration because of her extensive knowledge of the neurologic complications caused by vaccinations. Pet'r's Ex. 71 at 2. Dr. Schreiner highlighted that R.S. did not develop any other autoimmune conditions while under Dr. Schreiner's care. Dr. Schreiner credibly noted that the development of other autoimmune conditions, such as lupus, during the time she has treated R.S., would have been a signal that R.S.'s TM was caused by something other than her Prevnar 13 vaccine. Dr. Schreiner also noted that R.S. was originally tested for alternative causes of TM, such as infections and other autoimmune conditions including lupus, and the tests yielded negative results. *See* Pet'r's Ex. 10 at 44, 858–59; Pet'r's Ex. 9 at 3, 13. R.S.'s affirmative lack of substantiated alternative causes, both at the time of onset and in the years following, supports Dr. Schreiner's opinion that the PCV 13 vaccine caused R.S.'s immune-mediated TM.

Petitioners' claim is further supported by Dr. Steinman. He provided evidence in support of his assertion that R.S. experienced an immune-mediated reaction to the PCV 13 vaccine in her spinal cord, indicative of a molecular mimic. He has shown that the Prevnar 13 vaccine contains phosphoglycerol that induces antibodies (an immune response) to that phospho polar head group, which then cross-reacted with the same phospho polar head group of the phospholipids of the myelin in the spinal cord to cause R.S.'s TM. Dr. Steinman's reliance on R.S.'s medical records to show an immune-mediated response is persuasive. He noted that R.S.'s MRI results from April 2, 2013, showed damage to her C2–C4 spine, indicative of an autoimmune or immune-mediated, TM. Pet'r's Ex. 9 at 2–3. He also noted that R.S. yielded abnormal CSF results, but R.S.'s other testing did not reveal an infectious disease pathogenesis. Respondent's expert agreed that R.S. suffered an inflammatory, autoimmune or immune-mediated TM and has otherwise been unable to refute Petitioners' theory of cause and effect. *See* Tr. 153–54.

Additionally, the rapid development of R.S.'s condition post vaccination favors attributing causation to this specific trigger. R.S.'s PCV 13 vaccine was the only documented catalyst between her vaccination on March 18, 2013, and the onset of her TM on April 1, 2013. Petitioners' have presented evidence showing that prior to R.S.'s March 18, 2013 vaccine, she was able to pull herself up to standing and was meeting all developmental milestones. By April 4, 2013, R.S.'s condition had deteriorated to the point that she required assistance holding herself up and a special seat for feeding. *See* Pet'r's Ex. 1 at 5–6. Dr. Schreiner's opinion as R.S.'s treating physician, Dr. Steinman's expert opinion and accompanying medical literature, and the clinical progression of R.S.'s disease provides preponderant support for Petitioners' theory of cause and effect that is not

based on a temporal association alone. *See Grant,* 956 F.2d at 1148; *see also Hasler v. United States*, 718 F.2d 202, 205 (6th Cir. 1983) (finding that "[w]ithout more, [a] proximate temporal relationship will not support a finding of causation").

Petitioners have provided preponderant evidence that R.S.'s March 18, 2013 Prevnar 13 vaccine caused her TM via her proposed biological mechanism pursuant to *Althen* prong two.

D. *Althen* Prong Three

Under the third prong of *Althen*, a petitioner must show that the timing of the injury fits with the causal theory. *See Althen*, 418 F.3d at 1278. For example, if a petitioner's theory involves a process that takes several days to develop after vaccination, an injury that occurred within a day of vaccination would not be temporally consistent with that theory. Conversely, if the theory is one that anticipates a rapid development of a reaction post-vaccination, the development of the alleged injury weeks or months post vaccination would not be consistent with that theory. *See de Bazan*, 539 F.3d at 1352. Causation-in-fact cannot be inferred from temporal proximity alone. *See Grant,* 956 F.2d at 1148; *Thibaudeau v. Sec'y of Health & Hum. Servs.*, 24 Cl. Ct. 400, 403–04 (1991); *see also Hasler*, 718 F.2d at 205 ("[w]ithout more, [a] proximate temporal relationship will not support a finding of causation").

The parties generally agree that the time frame for developing a demyelinating condition following vaccination is between five- and forty-two-days post vaccination. *See, e.g.*, Pet'r's Ex. 22 at 10–12; Tr. 160:5–12. This time frame is well-supported by the medical literature. Indeed, Petitioners' reliance on the Bennetto and Scolding[95] article, which shows that the onset of ADEM post vaccination can occur within one day and three weeks or more, is persuasive. Pet'r's Ex. 44 at 3. Petitioners' position is further supported by the Schonberger et al.,[96] article which notes the onset time for GBS following the swine flu vaccination ranges from one to six weeks. Pet'r's Ex. 45 at 6–7. While Petitioners' submitted medical literature and testimony do not address the post-vaccination onset time for the development of TM specifically, it does provide a timeframe for the onset of comparable demyelinating conditions. *See, e.g.*, *E.M. v. Sec'y of Health & Hum. Servs.,* No. 14-753V, 2021 WL 3477837, at *42 (Fed. Cl. Spec. Mstr. Jul. 9, 2021) (comparing the onset time of GBS via molecular mimicry to the timeframe for small fiber neuropathy).

The record reflects that R.S. received the Prevnar 13 vaccine on March 18, 2013, and the parties agree that she experienced the onset of her TM on April 1, 2013, approximately thirteen days later. I am persuaded by Dr. Steinman's testimony in which he explained, based on the submitted literature and his specialized knowledge in neurology, that "thirteen days between [R.S.'s] immunization . . . would be right in the bullseye of when neuroinflammatory conditions are likely to [] manifest." Tr. 99:9–13. Respondent's expert did not submit evidence to refute this fact.

I find that Petitioners have presented preponderant evidence to establish that the onset of R.S.'s TM, an inflammatory demyelinating condition, occurred in a timeframe consistent with

[95] *See* Bennetto & Scolding, *supra* note 73.
[96] *See* Schonberger, et. al., *supra* note 74.

Petitioners' proposed theory of causation. Therefore, Petitioners have satisfied their burden under *Althen* prong three.

E. Alternative Cause

If a petitioner presents a prima facie case, the Federal Circuit has held that the burden of proof shifts to the government, and Respondent must prove that the "'injury . . . described in the petition is due to factors unrelated to the . . . vaccine.' 42 U.S.C. § 300aa-13(a)(1)(b)." *Knudsen,* 35 F.3d at 547. Yet, a petitioner's failure to prove any element of his prima facie case mandates that the Court deny entitlement. *See id.* Under such circumstances, the burden of proof does not shift to the respondent to establish an alternate cause for the petitioner's claimed injury. *Althen,* 418 F.3d at 1278; *see also Bradley v. Sec'y of Health & Hum. Servs.,* 991 F.2d 1570, 1575 (Fed. Cir. 1993).

In this case, Petitioners have established a prima facie case for compensation under *Althen.* Therefore, Respondent has the burden to prove R.S.'s injury was caused by something other than her March 18, 2013 PCV 13 vaccine. *See LaLonde,* 746 F.3d at 1340. However, Respondent has been unable to do so. Respondent's expert, Dr. McGeady, opined that R.S.'s preceding infections and illnesses caused her TM. Tr. 153–54, 160, 163–64. Yet, after extensive questioning, he admitted that, out of many potential preceding illnesses, he could not testify as to which one, if any, caused R.S.'s injury. He only vaguely noted that her TM was "triggered by something." Tr. 163–64. Respondent has therefore failed to identify any one condition that could have caused R.S.'s TM. Therefore, Respondent has failed to show by preponderant evidence that R.S.'s TM was caused by an alternative cause.

V. Conclusion

Petitioners have established by preponderant evidence that the Prevnar 13 vaccine R.S. received on March 18, 2013, was the cause-in-fact of her TM. Therefore, the evidence Petitioners presented has demonstrated entitlement to compensation. Accordingly, this case shall hereby proceed to the damages phase.

IT IS SO ORDERED.

s/Herbrina D. Sanders
Herbrina D. Sanders
Special Master